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SUPERFICIAL PUNCTATE KERATITIS*

A record of an epidemic of superficial punctate keratitis which appeared in Madras about May, 1928, and continued during the year that followed, embodying observations relating to the clinical appearances, biomicroscopy, epidemiology, aetiology and histopathology, of the disease, based on the investigation of over 900 cases

BY

LIEUT.-COL. R. E. WRIGHT, M.D., C.I.E., I.M.S.

PROFESSOR OF OPHTHALMOLOGY, MEDICAL COLLEGE, AND SUPERINTENDENT, GOVERNMENT OPHTHALMIC HOSPITAL, MADRAS

AND CO-WORKERS

SUPERFICIAL punctate keratitis was described independently by Adler, v. Carion, v. Reuss, and Fuchs, in 1889, and in its more usual aspects, it has been recognised clinically since that time.

It is represented in published accounts as an affection of the cornea and conjunctiva with an acute onset, attacking one, or less frequently both eyes, and characterised by the appearance of discrete opacities of the superficial layers of the cornea. These vary in size and number from a multitude of fine grey points only visible with a loupe to isolated spots easily seen with the naked eye. The epithelium at the affected points is commonly smooth, but may be raised; staining is variable, and actual vesiculation uncommon. The onset is like that of a mild conjunctivitis, and may be associated with catarrhal conditions of the respiratory tract, the

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corneal lesions appearing from a few days to a few weeks later. After a short time the eye becomes quiet and the opacities tend to disappear, but they may persist for upwards of a year or more, and exacerbations may occur. The vision is rarely interfered with to any great extent. The affection is not associated with iritis, but hypotonus may occur. It is most common amongst young adults, and recurrences are not observed.

A perusal of different records gives one the impression that the clinical features of the disease are liable to extensive variations and in its less characteristic manifestations it has sometimes, no doubt, found a place amongst the numerous descriptions of corneal affections of doubtful nature, in which isolated observations on morphological appearances are so confusing, in the absence of a knowledge of their cause. It is hardly to be expected that a composite picture of such an affection in all its manifestations should be available at present, as hitherto there has been no aetiological criterion to help in the diagnosis. That the disease might assume protean form was appreciated by many observers; Fuchs considered that superficial punctate keratitis and keratitis disciformis were probably of the same nature and were due to an unrecognisable organism. He also considered that there was a resemblance between herpes febrilis corneae and superficial punctate keratitis.

In 1911 Verhoeff made a detailed histopathological study of an eye affected by this disease (*Trans. Amer. Ophthal. Soc.*, Vol. XII, 1911). He regarded it as a neuropathic affection and considered keratitis disciformis to be of a similar nature. His paper constitutes a concise exposition of our knowledge of the condition up to that time, and forms a stage from which the present observations may well continue, as definite progress regarding the pathology or aetiology of the disease does not appear to have been made since. It was not very long, however, till Grüter identified herpes corneae febrilis with other forms of herpes simplex, and showed it to be due to a filter passing virus transmissible to animals. Since then Loewenstein, Lipschutz, Goodpasture, Levaditi, and numerous others have carried out investigations into the aetiology of these conditions, and their work constitutes a most important chapter in the progress of our knowledge of the so-called virus diseases. It is impossible for me to refer to the many authors who have contributed to these investigations nor, with few exceptions, will any attempt be made in this paper to quote references to the literature, since the necessary library facilities are not at my disposal. Those who are interested in the subject, and have facilities, may trace all the literature from the papers or authors quoted. It has now been established that herpes febrilis corneae (herpes simplex, dendritic ulcer), herpes labialis, herpes facialis

and herpes genitalis, are clinical manifestations of a condition due to a filter passing virus transmissible to animals, and capable of producing encephalitis in rabbits. Superficial punctate keratitis was, however, not generally looked upon as a member of the ultramicroscopic group, although, with the progress of knowledge in this field, the idea no doubt suggested itself to interested observers and actually may have been published without my knowledge. The herpetic affections of the cornea, which took on a new interest on account of this relation with the filter passing viruses, fell into two groups, herpes zoster ophthalmicus, and herpes corneae febrilis. They were clinically distinct, but had points in common. They showed relations with other conditions affecting the region of distribution of the fifth nerve. Paton, in his article in THE BRITISH JOURNAL OF OPHTHALMOLOGY, June, 1926, sums up the position as regards this group of affections up to that time. Whether these two conditions are different clinical manifestations of invasion by the same virus is a moot point, but until experimetal evidence in support of this hypothesis is very much stronger, one must give due weight to the differences which exist in the clinical pictures. Up to the present the determination of the specificity of a filterable virus is a very difficult matter, and before different clinical syndromes can be regarded as having the same aetiology, the production of reliable experimental evidence is necessary, for example, the fixation of rabies virus in passage rabbits, or the establishment of protection in distemper.

In the present article, I attempt to give an account of an epidemic form of keratitis in which, with the help of my hospital staff and some members of the laboratory of the King Institute of Preventive Medicine, Guindy, a fairly extensive investigation was conducted. It will perhaps be acknowledged that clinically, the disease presented resembles the superficial punctate keratitis of ophthalmic literature rather than any other well-known corneal affection. The occurrence of large numbers of cases in a comparatively short time afforded an opportunity of observing wide variations in clinical appearances, which presumably, were due to the same causative agent. The composite picture thus afforded, embraced not only different types of superficial punctate keratitis as referred to in standard works, but also such forms as described by Herbert (*Ophthal. Rev.*, Vol. XX, 1901) and Kirkpatrick (*Brit. Jl. of Ophthal.*, Vol. IV, 1920), the keratitis epithelialis punctata of Koeppe and keratitis disciformis of Fuchs. There was no real resemblance to herpes zoster ophthalmicus or herpes febrilis corneae, and although there is sufficient evidence to place the various manifestations of superficial punctate keratitis along with these diseases amongst the neurotropic ectodermoses of Levaditi, the occurrence of a distinctive group of clinical and pathological

changes constituting a third herpetic syndrome, is strongly in favour of the hypothesis that the causative virus in such cases is different, even if it is of the same type.

Clinical and Epidemiological Observations

Since Kirkpatrick described a variety of keratitis from this clinic in 1920, we have regularly, year by year, recognised and tabulated such cases. He regarded it as occurring in epidemic form in 1918-19 and recognised affinities, in some of its phases, with superficial punctate keratitis. He did not find an association with other diseases, although he remarked on the great influenza epidemic which prevailed about that time. There was not any increase in the incidence of herpetic affections.

The outstanding characters of this affection, which was locally called macular keratitis, were: the insidious appearance, without previous illness, of round grey spots in the superficial layers of a smooth, non-staining cornea, a tendency for these spots to thin out and become nebulous, showing a silk-like graining and to assume the appearance of complete or broken rings. The smaller spots were just visible to the naked eye, but large solitary forms might attain a diameter half that of the cornea. Kirkpatrick described three types of spots, small multiple, mixed large and small, the large spots being crenated or irregular, and solitary large spots. There was rarely any local discomfort or disability, unless the spots happened to be in the pupillary area. For the most part, one eye only was affected. We regarded this as an independent affection and saw a variable number of cases amongst about 20,000 out-patients annually.

1922	1923	1924	1925	1926	1927
28	18	33	109	67	14

Attempts made by Kirkpatrick and Cunningham, and subsequently by the latter worker and the author, to find an infective agent failed. Kirkpatrick considered the disease either parasitic or nutritional. The negative bacteriological findings were against the first hypothesis, the unilateral character against the second. He suggested a protozoal aetiology. He made the very important observation that there were numerous small granules in many of the epithelial cells, although, till now, the significance of this point was not appreciated. Since Kirkpatrick published his description,

I have had the apportunity of observing such types as he described with the corneal microscope. The smaller solid maculae appeared to be situated close below Bowman's membrane, and were not necessarily associated with any other change. The larger foci, on the other hand, approaching the disciform type, showed changes affecting the whole thickness of the cornea. The posterior surface of the cornea bulged into the anterior chamber. There were foldings of Descemet's membrane and deposits on the endothelium, for the most part pigmented in nature. I did not publish my observations on this condition, and it is unnecessary to go into further details here, because the changes which are hereafter described in superficial punctate keratitis, as seen by the corneal microscope, embrace those varieties which were formerly considered as an independent disease. In the year 1928, up to the end of May, there had been comparatively few cases of macular keratitis recorded in hospital; at the end of this month several private patients showed what appeared to be a similar condition, though it was atypical, inasmuch as there was a history of greater irritation. It was soon realised that we were dealing with a different type of affection, and as certain older cases subsequently gave a history of onset in May, the commencement of the epidemic may be placed about this month. During the next two months there was a great increase in the number of cases of keratitis in hospital: most of these were superficial punctate keratitis, but as we had not instituted a systematic verification by the corneal microscope, the figures for these months can only be taken as approximations and have not been included under the head of superficial punctate keratitis in the usual returns of the hospital for 1928. Only 801 cases are so included, but all of these were verified by the corneal microscope when necessary, as they occurred, from the month of August onwards. For 1929, the number of new cases up to the end of May was 122, giving a total of 923, to which figure reference will be made throughout this paper, unless otherwise stated.

Simple clinical type.—An early case, which may be taken as a typical clinical example of the simpler uncomplicated varieties of this affection, occurred in a member of our refraction room staff. Without any previous indisposition, a conjunctival hyperaemia made its appearace in the left eye. There was no lacrymation, or photophobia, except in strong light. The vision was not blurred, nor was there a conjunctival discharge. From the observer's point of view the chief feature was the unilateral hyperaemia. The patient had very little discomfort and went on with his work. The naked eye appearance of the cornea was apparently normal. At one place there was a little irregular elevation of the limbus; there was no staining. With the corneal microscope, the elevated portion

of the limbus showed oedema and engorgement of the vessels, and a few slightly more raised points. Close by, on the cornea, there were a few small rounded opacities. Gradually the number of opacities increased and in a couple of days they had invaded the pupillary area, where they were just visible to the naked eye. The vision, then, for the first time became blurred. The older spots tended to thin out as newer ones advanced on the cornea. The patient wore a shade over the eye at first, later a wet pad; dionine was given. In a month there was nothing abnormal to be seen with the corneal microscope.

This case was considered sufficiently like the superficial punctate keratitis of standard works to justify us in regarding it as such, although the absence of previous indisposition, the presence of limbal elevations, and uneventful progress to a speedy recovery, were noteworthy. The later stages, when the puncta became thinned out and nebulous, suggested macular keratitis, while the limbal elevations suggested the appearance described by Herbert in the Bombay epidemic.

With the observation of large numbers of cases it became clear that there were enormous variations in the clinical course of the disease, but certain features were frequent and prominent, and served as guides to the nature of the affection, even without recourse to the corneal microscope. The affection of the eye appeared without an antecedent febrile or catarrhal disturbance. The onset was suggestive of a mild catarrhal conjunctivitis in the great majority of cases. In practically every case, at least a history could be obtained of a slight change in colour of the affected eye. Sometimes this hyperaemia of the conjunctiva was only discernible when the patient was viewed at arm's length in a good light. The patient sometimes was unaware of this redness and was informed of it by friends or observed it in the looking glass. It may well be imagined that such a mild state might easily be missed, and should corneal opacities be detected later, it might readily be assumed that they developed in a purely non-inflammatory manner, as we had supposed to be the case in many of the attacks of Kirkpatrick's macular keratitis. There was every variation from this mild hyperaemia, to the rarer cases, where there was oedema of the lids with chemosis, and an appearance which suggested the onset of a very acute infective conjunctivitis. Discomfort was inconspicuous in the milder attacks, but definite irritation, lacrymation and photophobia were present in the cases which showed a more marked degree of hyperaemia. Blurring of the vision, if present, was usually associated with opacities of the cornea in the pupillary area. There was no conjunctival discharge in uncomplicated cases. In the majority of patients the disease was unilateral, in six only were both eyes affected. There was not a single instance of associated

skin affection of a herpetic type, or of neuralgic pain in the area of distribution of the fifth nerve. It frequently happened that the limbal region was definitely swollen and oedematous and that it showed small elevations. In a few cases there were similar little elevations on the bulbar conjunctiva at a distance from the limbus, but they were not identified on the palpebral conjunctiva. These elevations appeared as small translucent papules in the light reflex, not as grey infiltrated points. The cornea showed a range of appearance from perfect smoothness and apparent transparency, even with the loupe, to invasion with large solitary disciform opacities. Sometimes the corneal transparency was due to the fact that the puncta had not yet developed; at other times, the opacities were so fine, that they could only be detected with the microscope. The longest interval observed between the onset of conjunctival hyperaemia and the appearance of spots was six days but it is quite possible that longer periods may elapse. On the other hand in some cases corneal opacities were seen on the first day of occurrence of conjunctival hyperaemia. There is thus a considerable variation in this respect. The most common condition was that in which numerous small rounded grey spots were visible either to the naked eye or the loupe. They did not always stain, nor was the epithelium always elevated. Out of 224 cases tested with fluorescine, 88 did not stain. In the majority of cases, some of the puncta at least, showed slight epithelial elevation. The number of spots varied enormously. Their characters will be dealt with further when describing the corneal microscope appearances. A lowering of the tension was not a noticeable feature, although, in some of the severe attacks, there was a slight fall. Apparent recrudescences were occasionally observed, but relapses were not noted. The duration of the corneal opacities varied from a week to over a year. In the great majority of cases they disappeared completely in less than two months, in some cases, they remained as faint rounded macular spots, occasionally annular, which were possibly of a permanent nature. The cases could not be followed up for a sufficient length of time to be definite on this point. In rare instances there were dense, white, cicatricial remains which obviously were permanent. Corneal sensibility was nearly always within normal limits. Even in patients who showed severe lesions, the corneal sensibility was preserved. In the vast majority of cases the iris appeared to be normal, the pupils being symmetrical, and the reflexes unchanged.

In two of the bilateral cases, both eyes were attacked at the same time, but evidently a variable period might elapse before the second eye was affected, as an interval of fifteen days was noted in one case. As increasing numbers of cases were observed, it became evident that there were transitional forms of corneal involvement,

ranging from fine granular or curdy superficial opacities of an evanescent character, to large solitary foci of the disciform type affecting the whole thickness of the cornea, and associated with a greater or lesser degree of anterior uveitis. The condition which we had been accustomed to designate macular keratitis (Kirkpatrick), was apparently the same affection in which the onset had been unobserved, or perhaps had been atypical, and only the larger and more persistent types of opacification were seen, and, for the most part, in their later quiescent stages. The small, round macular forms, described by Kirkpatrick, are similar to the later stages of the larger, rounded spots of superficial punctate keratitis visible to the naked eye; whilst the larger irregular forms, and solitary foci described by him, merge imperceptibly into what is usually regarded as keratitis disciformis. The larger foci are usually few in number, but one cannot infer that the condition originated with a small number of spots, from the fact that there happen to be three or four foci of 1-2 mm. in diameter, or because there is a solitary opacity of double this size. Such large foci take time to develop, and usually represent the later stages of a corneal condition in which, at first, there were more numerous smaller opacities, one or two of which had outgrown and outlived the others.

I was interested to see quite recently that Prof. Salzmann, of Graz, had traced this transition from superficial punctate keratitis to keratitis disciformis. I gather that his experiences with regard to transitional forms are very similar to ours in Madras with macular keratitis (Kirkpatrick). Prof. Salzmann observed 50 of these transitional forms in 16 years at Graz, but not a single typical case of superficial punctate keratitis, although the latter was practically epidemic in that part of the world in 1889. He regards them as different manifestations of the same disease, and considers that local and temporary differences occur which explain his observations. The local variations of the disease, he had not observed elsewhere, and the typical superficial punctate keratitis, so common in 1889, was not seen during the period of his observations.

Typical dendritic ulceration of the cornea was only seen thrice during the period which our observations cover. In one case, that of a British soldier, there was a history of malaria immediately preceding the onset. The second, in an Indian patient, was associated with herpes labialis, the third was definitely diagnosed, but the case sheet was lost. Presumably, if one could observe herpes febrilis corneae in epidemic form, considerable variation would be found in the nature of the corneal lesions, from simple vesicles to complicated dendritic types, some of which might resemble superficial punctate keratitis. The association with a

febrile disturbance, herpes febrilis of the skin, and the greater severity of symptoms would perhaps be outstanding features.

Only one other case of herpes labialis was observed during the time under consideration, and in that there were no corneal manifestations; herpes zoster ophthalmicus was noted five times.

Treatment

The average patient improved rapidly when the eye was kept covered with a moist boric pad under an eye shade, or bandage, and treated with dionine drops twice daily and atropine ointment at night. Other simple remedies such as hot fomentations were employed from time to time. In more protracted types, additional measures were resorted to, as mentioned in connection with special cases. Treatment, on the whole, was along general lines, and there is little worth noting except that in those cases in which the eye was kept covered from the beginning the improvement was more rapid than in the others. To be more accurate, the most prolonged lesions were seen in patients who had not kept the eye occluded from the commencement.

The prognosis may be regarded as very good; only three patients showed a definite decrease in visual acuity. There may, of course, have been others who did not report.

Apparently one attack gives protection for a time, as recurrences were not observed.

The disease was most common in males between 20 and 30 years of age.

The relative frequency at various ages, and in the two sexes, as well as the influence of season and climate, are shown in the following tables:—

TABLE I.

Influence of age and sex.

Sex.	Age periods.							
	1-9	10-19	20-29	30-39	40-49	50-59	60-69	Total.
Males	3	113	413	167	55	16	5	772
Females	4	43	55	27	9	11	2	151
	7	156	468	194	64	27	7	923
Percentage	0·76	16·9	50·7	21·02	6·93	2·93	0·76	

Ratio of males to females attending hospital 1·8 to 1.

TABLE II.

Climatic conditions 1928-1929.

Year and Month.	No. of cases of superficial punctate keratitis.	Mean monthly temperature	Humidity.	Rainfall in inches.
1928				
May		89·6	61%	0·03
June	40 (Approx.)	89·0	54%	0·24
July	50 ,,	86·0	62%	3·27
August...	121	83·9	69%	4·70
September	242	83·7	74%	8·18
October	146	81·2	82%	20·81
November	133	79·4	77%	6·64
December	160	77·0	76%	4·24
1929				
January	58	75·8	78%	1·87
February	26	77·1	75%	6·41
March	16	80·5	73%	0·01
April	10	84·1	74%	0·55
May	11	88·3	65%	0·75

Race did not seem to influence the incidence; Europeans, Hindus, Muhammadans, appeared to be equally liable to attack.

The method of spread was not obvious. One individual working in an office with half a dozen others might be attacked, whilst the remainder escaped. In an orphan school in my medical charge, where 200 Anglo-Indian boys and girls, of ages ranging from four to eighteen, live under dormitory conditions, there were less than a dozen attacks in 1928. The cases recorded from this school are not included in the 923.

Trauma is noted in the history of a large number of cases and it is quite likely that it favours an attack.

Distribution

As regards the distribution outside the city very little information was forthcoming. The disease was known to be occurring simultaneously on the west coast, in Bombay, and over the intervening Mysore plateau. It was not in evidence in parts of Hyderabad, the north of the Madras presidency, in Calcutta or Lahore. This information is derived from ophthalmologists who had seen the disease in Madras, and subsequently communicated with me. One may consider that the disease was making its appearance all over the south of the Peninsula with comparatively greater frequency than usual, but the data which are available are insufficient to allow of any definite opinion being expressed on this point.

Superficial Punctate Keratitis as an Epidemic Disease

There seems to be very little doubt that we were dealing with superficial punctate keratitis in epidemic form, similar to the epidemic observed by Herbert in Bombay in 1900. Evidently when the disease appears in epidemic form, it shows the more typical characters set out above. These resemble the original description of the disease in 1889, when there were so many cases that it may be regarded as having been epidemic. Kuffler, of Berlin, has observed cases of superficial punctate keratitis occurring in such numbers as to give him the impression that it was in epidemic form. That the typical superficial punctate keratitis may appear sporadically is well-known, and supported by numerous observations. My notes include a few quite distinct cases occurring at long intervals during the years preceding the present epidemic. That the disease probably occurs in atypical forms, both sporadically and endemically, is suggested by the experience of Salzmann referred to above, and by our local observations in connection with the variety of keratitis described as a separate disease by Kirkpatrick. There seems to be much in favour of the view that the latter disease is but a variety of superficial punctate keratitis, which occurs as an endemic disease, and forms a transition stage between acute epidemic evanescent keratitis, and solitary sporadic cases of keratitis disciformis.

Corneal Microscope Observations

The commonest change was the appearance to a greater or lesser degree, of small grey points of opacity in the superficial layers of the cornea. There did not seem to be any characteristic distribution, nor were the points of invasion necessarily confined to the cornea. It was frequently observed that the limbus was definitely raised, and showed vascular engorgement and oedema, with small elevations not only at the limbus itself, but at a little distance from it on the bulbar conjunctiva. Such cases often showed but one or two corneal spots close to the most affected portion of the limbus. Later, an increase in the corneal deposits sometimes occurred, involving the whole of the corneal surface within a day or two. Cases in which the involvement of the limbus was conspicuous we came to speak of as of a "limbal type." A patient might be under observation for several days before the full crop of superficial opacities developed. I did not concern myself much with the limbal or conjunctival spots, except to verify their existence side by side with the characteristic corneal lesions and their definite occurrence in cases in which the limbal type preceded a corneal invasion. This point is of interest in view of the fact that Verhoeff held Herbert's cases to be different from true superficial punctate keratitis, inasmuch as they showed limbal and conjunctival invasion. One had

only to watch a number of early cases to see that there was a regular march in the appearance of superficial points of invasion from the conjunctiva to the limbus and over the limbus to the cornea. The corneal lesions varied enormously in size and number, so that there did not seem to be anything typical in either of these features. The number of points varied from one to hundreds; they might be disposed altogether towards the periphery, or in one quadrant, while in some cases they were practically confined to the centre of the cornea.

The various types of opacification may be treated in more detail. A common variety gave the impression of a very fine curd when seen with the corneal microscope. These were referred to as fine curdy deposits. They were ill-defined in outline and were so small as to be invisible to the naked eye. The individual points which ran together to form the more obvious curdy masses were not well demarcated even with the high power. Sometimes the opacifications were more uniform, like a fine opaque precipitate, rather than a curd. These changes were situated in the epithelium, and possibly extended under Bowman's membrane, but this could not be determined with certainty without first removing the epithelial layers. The fine curdy deposits frequently raised the epithelium, so that eminences were visible in the zone of the specular reflection. Staining of the spots was sometimes noted, but more often not, although there might be a diffuse fluorescence of the epithelium. In certain cases, these fine curdy deposits disappeared altogether in the course of ten days or so. The shortest period in which they were observed to fade away was one week.

Another type of opacity was of a discrete angular type, sharply marked, and densely opaque, and sometimes visible to the naked eye. Most commonly the spots were round, all sizes and densities being seen, from minute circumscribed points, like tiny colonies on a culture medium, to large fuzzy, steamy-looking discs, of 2 mm. or more in diameter. The large discs were presumed to have developed from smaller discs; in a few cases this process was actually observed. An interesting feature of some of these rounded types (and indeed of some of the angular types too), was the transition to annular forms. Even where they were of small size, spots were observed with a clearer centre, and dense periphery. In fact, in the smaller varieties, sometimes the ring was very sharply marked off from the clear centre and the surrounding cornea. Evidently these forms arose from a desquamation of the heaped-up centre of the minute papule, which constituted the initial lesion, and apparently were disposed chiefly in the epithelial layers. For the larger rounded opacities of 1 to 2 mm. in diameter such an explanation of the formation of ring forms does not hold. In these, as the condition progressed, the superficial focus became larger and less

defined, spread deeper and definitely involved the superficial substantia propria. Later the epithelial centre became clearer, as also did the opacity of the anterior layers of the substantia propria, so that the more opaque periphery stood out in contrast to the clearer centre. Sometimes there was a central point of greater opacity, with perhaps two alternating zones of greater or lesser opacity outside this. It did not seem to be essential that an individual spot should form a ring by peripheral extension; the process might take place by a clarification of the centre, the original outline of the solid round spot remaining the same. The larger spots did, however, tend to spread, and fade off into the surrounding cornea in an oedematous haze. Large isolated infiltrations, of 3 mm. or more in diameter, of the disciform type, involved the whole thickness of the cornea. The epithelium might remain perfectly smooth and level in such cases, and stain in a faint diffuse manner, but more usually it was granular or rough. Swelling of the substantia propria manifested itself in the optical section by extensive humping of the internal limiting surface. In such cases the formation of zones, or rings, of greater or lesser density, depended on the altered refraction of the deeper layers, rather than on any absorption of the central epithelial layers. It is hard to say what the actual opacification of the epithelium is due to, as the histopathological investigation did not show leucocytes in the epithelium, whilst epithelial sheets stripped from the cornea showed definite spots corresponding to similar spots just below Bowman's membrane. Presumably, the degenerative changes taking place in the epithelial cells are sufficient to determine the opacity of the smaller lesions. Loss of surface epithelium was not a feature of the disease either in the smaller foci, or in the larger, as it presumably is in herpes febrilis. Invasion of the substantia propria was more marked the larger the individual opacities became, till it reached a maximum in the big solitary disciform types. In medium sized opacities, it was possible to trace the ring formation from the earliest foci right up to the complete rings, broken rings, and mutton chop forms which were previously recognised in macular keratitis (Kirkpatrick): so that one was led to the conclusion that this condition was a later stage of superficial punctate keratitis in which, for some reason, early acute manifestations had been absent or missed. Evidence in support of this view was the fact that patients used to appear during the epidemic with typical macular keratitis, who, when questioned, admitted to having had a slight redness some time before. With our present experience of superficial punctate keratitis it is difficult to understand how we can have observed up to 100 cases in a year of this macular keratitis, without having seen the initial stages, but it is likely that when the disease is occurring epidemically, the early

conjunctival hyperaemia is a more prominent feature. It should also be noted that even during the epidemic we saw cases in which the patient's first complaint was the dimness of vision due to opacities in the pupillary area, and these were of the small superficial punctate type. The freedom from irritation, the appearance of rounded opacities, and ring forms, which were usually unilateral and visible to the naked eye, were regarded as characteristics of the condition described by Kirkpatrick, but some of the cases which we considered typical of that affection, were observed both before, and during the epidemic, with considerable irritation and photophobia. At the same time, cases were presenting themselves with mild conjunctival irritation which, without observation by the corneal microscope, would have passed unnoticed.

The deeper changes.—Even in the mildest types of the disease, in which the initial conjunctival hyperaemia was not noticed by the patient, and the opacities were small and sparse, causing but a slight dimness of vision, there was nearly always some trace of a fine deposit on the endothelium. From this condition, there were numbers of variations up to the most extensive folding of Descemet's membrane and large pigmented deposits. In the less severe cases there was usually a fine white, or pigmented deposit, with or without a few foldings of Descemet's membrane. In all cases of the disciform type there were extensive foldings, and, outside the thickened zone, there were marked pigmentary deposits. There were, however, exceptional types and in a few cases, in which there was very little irritation, and the corneal opacities were small, round, and discrete, there were round translucent yellow keratic precipitates, the deposits being larger than the superficial opacities and easily visible to the naked eye. The aqueous too, in some mild cases, showed variations from an increase in relucency to obvious floating particles, pigmented and non-pigmented. In one typical case, the pupillary border showed a Koeppe's nodule which gradually disappeared while the patient was under observation. Except in this isolated case, the iris did not show evidences of disturbance. The retrolental space and vitreous sometimes showed fine pigmentary deposits similar to those seen on Descemet's membrane, but there was never any gross change observable in the vitreous with the microscope, or with the ophthalmoscope, such as extensive dust-like opacities, although of course, it was impossible to examine the posterior segment in the more severe types.

The corneal nerves did not show any constant changes. In certain cases a nerve would appear to be unduly prominent as it approached an opacification, but after numerous observations I was unable to say that there was a demonstrable lesion.

The endothelium was sharply defined in a good many cases, and

bedewing was certainly not a common feature, although sometimes it was present. Craters varied considerably in numbers in different cases. In some patients it was surprising how rapidly the superficial opacities, fine flocculent endothelial deposits, and folding of Descemet's membrane disappeared. In one case, this picture, seen by me on the fourth day, disappeared on the eleventh, and the eye was apparently normal to the corneal microscope on the sixteenth. In a certain number of cases the epithelial opacities cleared up, but grey spots remained in the superficial layers of the substantia propria; as far as one can see, these may be permanent. It is difficult to gauge the frequency of such a result as it was impossible to follow up hospital cases for long periods. Probably the vast majority of the smaller types of opacities cleared up absolutely, but at least six cases were known in which spots persisted at the end of a year. In one bilateral case the distribution was such as to give an appearance resembling a Groenouw's nodular dystrophy. The cornea was somewhat insensitive, but of course there was not a familial element. This case impressed me with the fact that not only Groenouw's dystrophy, but also other conditions might be simulated by the various late appearances following a superficial punctate keratitis. Even in cases where opacities, larger or smaller, persisted for months, loss of substance with dense leucomatous scarring was not noted during the period of observation, except in the case of one of our own nurses. She had a severe attack with marked irritation, and a group of five round spots, the largest being 2 mm. in diameter in the pupillary area. The largest spot was raised, became exfoliated at the centre and formed a definite ulcer involving Bowman's membrane and the superficial layers of the substantia propria, eventually leaving a depressed area in the anterior surface of the cornea. It is more than likely that the late opacities of the small rounded type are situated just below Bowman's membrane, and that Bowman's membrane and the epithelium are by this time intact, the original infection penetrating it, as suggested by Verhoeff, through the nerve apertures. Relationships with the more vesicular lesions of herpes febrilis might be traced in cases in which the opaque epithelium becomes heaped up to form a papule, then a vesicle, which bursts by desquamation at its centre, and forms the superficial variety of ring, which at this stage shows staining. There were also one or two cases of true vesicle formation. If one considers that the essential lesion of a herpes febrilis corneae is a simple vesicle, then there must occur isolated cases where the differentiation is practically impossible. The most representative lesion of herpes febrilis is said to be the dendritic ulcer, and the nearest approach to this condition which was observed was where a linear group of punctate opacities with one or two lateral offshoots

desquamated in parts and stained in a very suggestive way; but it did not stain throughout, and the symptoms were not so severe. In one of our experimental cases, where superficial punctate keratitis was transmitted to a man, a similar running together of small grey foci produced a dendritic appearance, which seen by retro-illumination, was exceedingly like a healing dendritic ulcer. The deep changes which were seen in two true dendritic ulcers which occurred during the epidemic were no more severe than in superficial punctate keratitis and could not have been used to differentiate the condition.

Summary

Just as in the case of the naked eye appearances the changes seen with the corneal microscope are diverse; numerous features were seen which might have been regarded as isolated phenomena and so described had they not been observed in their proper setting, and recognised as different manifestations of the same aetiological entity. In publications on corneal microscopy, there is a tendency to describe isolated phenomena as such, not necessarily in their proper environment, and this feature often tends to obscure the aetiology. The study of a disease like superficial punctate keratitis in epidemic form, in all its phases, shows that there may be the greatest diversity in the lesions of the cornea as regards their biomicroscopical appearances, although the initial and essential change, which is a localised opacification immediately on either side of Bowman's membrane, is probably common to all. Similarly Descemet's membrane and the endothelium may show a great variety of changes, and the evidences of abnormal constituents in the aqueous fluid, may vary in character from an increase in relucency to gross pigmented and unpigmented keratic precipitates.

Individual Cases showing exceptional or interesting features

1. *Long duration, marked keratic precipitates, untreated during early stages.*

Mr. H. P. W., aged 30 years, European, male, first seen on January 10, 1929, noticed that the left eye was red about a month before. He played cricket daily during the Christmas holidays. The eye did not trouble him, and he thought the redness was kept up by glare. The sight became slightly blurred, the corneal microscope showed small round superficial punctate spots, with larger deposits of amber, translucent keratic precipitates. He had to play in another important match and would not have a bandage or atropine. About January 15, treatment was started with atropine, dionine, and bandage. The precipitates remained unchanged up to March. During the latter half of March, he was given milk injections and a subconjunctival cyanide injection. The precipitates cleared within a fortnight and eye was apparently normal at the end of April.

2. *Bilateral case with centrally disposed rounded spots.*

Mr. L., Indian, male, aged 30 years, had a bilateral attack in July. The spots in each eye were small and round and disposed about the centre of the cornea in

considerable numbers. He would not have atropine or a bandage, but wore dark glasses and used dionine. The spots gradually became more nebulous, but interfered with vision. He was given irrigations of normal saline, or saturated magnesium sulphate, and dionine drops, regularly for weeks. He also had sub-conjunctival injections of normal saline. I saw him from time to time in consultation. He still showed a number of round nebulous spots, visible to the naked eye, about the centre of each cornea, a year after his original attack. The corneal sensitivity was normal. He complained that his vision was blurred, but he still retained 6/6 in each eye. If seen for the first time at this stage the condition might readily be mistaken for some other affection.

3. Long duration, dense scar, loss of corneal substance, interference with vision.

Miss de L., Anglo-Indian, aged 31, had an attack in the left eye July, 1928. There were three large rounded opacities at the centre of the cornea. These were raised, and stained with fluorescine. One increased in size to about 2 mm. in diameter. There was definite loss of epithelium and considerable irritation with marked folding of Descemet's membrane. In spite of atropine, dionine and bandage, the condition improved very slowly, and nine months later, three annular opacities remained. The central one was laminated, showing several concentric rings. The optical section showed a definite depression of the anterior corneal surface. The larger spot was near the pupillary area and the vision dropped from 6/6 to 6/18, but was improved with a cylinder to 6/9.

4. Deep changes, well marked, Koeppe's nodule.

Major H., European, aged 40 years. A crop of very fine curdy opacities developed on the cornea two days after onset. These disappeared in a week under atropine, dionine, and bandage treatment, but a most marked folding of Descemet's membrane (the most extensive observed in the whole series), was seen on the tenth day. This had largely subsided two days later, and instead, there were a number of large, rounded, pale greyish deposits of keratic precipitates. The corneal surface was clear by this time except for three small opacifications near the limbus. A rounded, amber-coloured, semi-translucent nodule (Koeppe's nodule), appeared near the pupil border on the iris face, and disappeared again some weeks later while the eye was under frequent observation. The eye was apparently normal in 8 weeks, all traces of the anterior uveal disturbance having disappeared.

5. True vesicle formation.

Capt. H., Indian doctor, aged 41 years, noticed slight hyperaemia of right eye when looking in his mirror. Four days afterwards, it got irritable. On the 12th day, when first examined at Hospital, the cornea showed a number of superficial opacities, with a definite vesicle in the inferior nasal quadrant. There were a number of very fine white deposits on Descemet's membrane, and a single large lardaceous keratic precipitate. The endothelium was sharp and distinct. The eye appeared normal within a month.

Note.—Only two cases were seen with true vesicle formation, *i.e.*, bullae. The papillary elevations of epithelium, no doubt, in certain cases, were raised above a small fluid accumulation, in or just beneath the epithelium, and when the summit exfoliated, there was a staining central abraded area which subsequently appeared under the microscope as a paler centre bounded by a more opaque ring.

6. Transition to the macular keratitis type.

B., Anglo-Indian, aged 22, was seen at the hospital with typical superficial punctate keratitis of the right eye on December 9, 1928. On February 15, 1929, he reappeared, and was regarded in the out-patient department as a typical case of macular keratitis Kirkpatrick), with a smooth cornea showing moderately large opacities of the annular type.

This class of case was not very uncommon.

7. Transition stage between macular and disciform types.

R. M., Indian, male, aged 26 years, had irritation of the right eye for 10 days. He showed a number of fairly large rounded spots on the lower three quarters of the

cornea. One of these showed a central zone somewhat clearer like an early ring-form. Below, there was a large dense spot of disciform type paler above, denser below, giving a crescentic effect. The epithelium overlying this disciform opacity was steamy. There were folds of Descemet's membrane and deposits of pigment on the endothelium.

8. Marked conjunctival disturbance, chemosis, simulating an early gonorrhoeal ophthalmia.

M., European, male, aged 24 years, was seen in consultation because of oedematous swelling of lids and chemosis of the conjunctiva of 12 hours' duration. Gonorrhoeal conjunctivitis was suspected by his doctor. There was very scanty discharge; smear preparations from the conjunctival epithelium did not show any organisms. Next morning the corneal microscope revealed fine rounded opacities all over the cornea. With atropine and bandage he was well in three weeks.

9. Disciform type.

In X., European, male, aged 40 years, the cornea showed a few small superficial dots, one much larger about 3 mm.; the eye was irritable. The surface epithelium over the larger disciform opacity was sodden and looked granular, and was very slightly raised; it stained in a diffuse way. The cornea was thickened and its posterior surface showed bulging in the optical section. The centre of the bulge could not be observed, but there were folds of Descemet's membrane near its periphery and pigmented deposits on the endothelium.

Several cases of this type were observed, one with a 5 mm. central disciform opacity, over which the epithelium, although sodden and rough, showed no breach of continuity. The smaller disciform types pass imperceptibly into the larger macular types, and they both affect the whole thickness of the cornea. Of these the smaller varieties tend to develop into annular forms.

10. Limbal type.

B., Indian, male, aged 19 years, had slight irritation of right eye for six days. There were few small grey spots on the cornea near the limbus above and below. Just outside the limbus the dilated vessels formed prominent radiating lines. Between the vessels and the cornea the limbus was raised into an elevated rim, bounding the cornea, which carried several more prominent translucent points, best appreciated in specular reflection. There were also raised points of the same nature some distance from the cornea on the bulbar conjunctiva.

11. Transition to macular keratitis and apparent connection of nerves with opacities.

G., Indian, male, aged 21 years, developed superficial keratitis, left eye, on October 28, 1928, with fine spots on cornea. He remained away 15 days and when next seen, he had a series of round spots, diffuse and nebulous, with perfectly smooth epithelium, of the smaller solid macular type, as contrasted with the larger ring, or disciform types. The deep surface of the cornea showed nothing abnormal. The nerves were easily seen, more opaque than usual, and in the case of one spot, a nerve filament was definitely traceable to the deep aspect of the spot. Corneal sensation was normal.

12. Transitional stage between superficial punctate and macular types, with marked changes in the aqueous.

S. P., Indian, male, aged 30 years, was seen on October 12, 1928, with a typical attack. There were numerous superficial spots, but three larger ones in upper and outer quadrant, staining faintly. Seen again on October 27, 1928. The eye was in the quiescent stage; the three spots seen before were now larger and of macular type; two were superficial. Behind one the whole cornea was thickened; the posterior surface of the optical section projected backwards. There were very fine deposits on the endothelium, and fine floaters in the aqueous. Immediately behind the larger opacity there were folds in Descemet's membrane and some pigmented deposits. This type was not uncommon and showed similar deep appearances to those observed with the corneal microscope in the varieties of macular keratitis with larger opacifications which had been seen in previous years.

Laboratory Investigations

Cultures were made on a variety of ordinary media, including Sabouraud's, from fresh material collected from 36 different recent cases, and incubated aerobically and anaerobically. The bulk of the tubes showed either no growth or infrequent organisms, known or unknown. No constant organism could be isolated. Slide preparations from scrapings of corneal epithelium, taken at the same time, were fixed, wet and dry, and examined microscopically : in these no predominant organism could be detected . An encapsulated organism, such as that described by Herbert, was not seen. Full details of all the cultivation work need not be given, as it proved negative. It will be sufficient to state the general procedure.

Cases of under a week's duration were selected in the out-patient department. They were verified with the corneal microscope. Only those with numerous definite opacities were chosen. The selected eye was cocainised and thoroughly irrigated with sterile saline solution for about two to three minutes, then cocainised and irrigated a second time. Thereafter with a speculum in position the epithelium was gently rubbed off with a Bowman's needle. Large numbers of planted tubes and slides were handed over to Dr. Theodore, of the King Institute of Preventive Medicine, Guindy. Dr. Theodore and Col. King verified the negative findings both cultural and microscopical in so far as organisms known or new were concerned.

Dark Ground Observations

Preparations from recent cases proved negative.

Histopathological Observations

Method of obtaining material.—It was found that the epithelial layers slid off Bowman's membrane more readily when obtained as above, in those areas where the punctate deposits were most numerous. It is, however, possible with such treatment, and a little care, to peel large areas of the epithelium right off Bowman's membrane even in normal eyes. This loosening and detachment of the whole thickness of the epithelial layer is not an uncommon event in the preparation of cataract cases for operation, by the irrigation method. This fact was made use of in obtaining large whole thickness sheets of corneal epithelium, both of affected and normal eyes, for subsequent histopathological examination.

After preliminary irrigation, the epithelium was first detached from Bowman's membrane over a short linear area, and then gradually peeled off with the flat or shaft of the needle, aided by the irrigator. It is thus possible to obtain pieces considerably over five sq. mm. Such sheets when floated out in normal saline, and examined with the binocular dissecting microscope, showed the

punctate mottling well. In patients from whom they were removed, opacifications corresponding to those on the epithelial sheets were still observable in or just beneath Bowman's membrane.

No harm ever appeared to result from denudation of the corneal epithelium by this method, nor from the scraping of the epithelium in order to obtain material for making cultures and slides.

Whole thickness sheets of corneal epithelium obtained as above were taken from recent cases of superficial punctate keratitis, and also from normal eyes. Twelve specimens of the former were prepared, and eight of the latter. The epithelial sheets were floated out in normal saline and examined under the binocular microscope so as to verify the presence of punctate spots in the one case, and uniformity in the other. They were then spread on slides, and while maintained flat with a superimposed slide, held lightly in position with thin rubber bands, were fixed in Zenker's fluid or methyl alcohol. The Zenker specimens were washed, and after graded dehydration in the usual way, stored in 80 per cent. alcohol; the others were transferred with one change. In the hope of finding evidence of cell inclusions it was determined to adopt methods such as were applicable to the staining of Negri bodies in sections of brain, a technique with which I had previous experience. For both diseased and normal epithelial preparations the following stains were used:

Haematoxylin and eosin Haematoxylin and van Gieson Mann's stain	For Zenker fixed tissue.
Leishman's stain Giemsa's	For alcohol fixed tissues.

The whole thickness epithelial sheets were much more difficult to stain satisfactorily than sections. After a number of failures to get satisfactory detail with the Mann's stain, Leishman, or Giemsa, successful staining was obtained with haematoxylin and eosin. The tissue was treated with ferric alum as a mordant, then overstained with haematoxylin, and differentiated under the microscope. In this way, the process could be controlled and a satisfactory haematoxylin staining obtained.

Looked at with the naked eye when stained thus, or for that matter by other staining methods, the diseased epithelium showed paler areas representing the opacities. These areas, when examined under the low power showed a thinning out of the epithelial layers with actual complete absence in some cases. The epithelial cells at these sites had evidently lost their normal staining characteristics and took up the stain feebly and atypically. There appeared to be a breaking up of the cell body and fragmentation of the nucleus

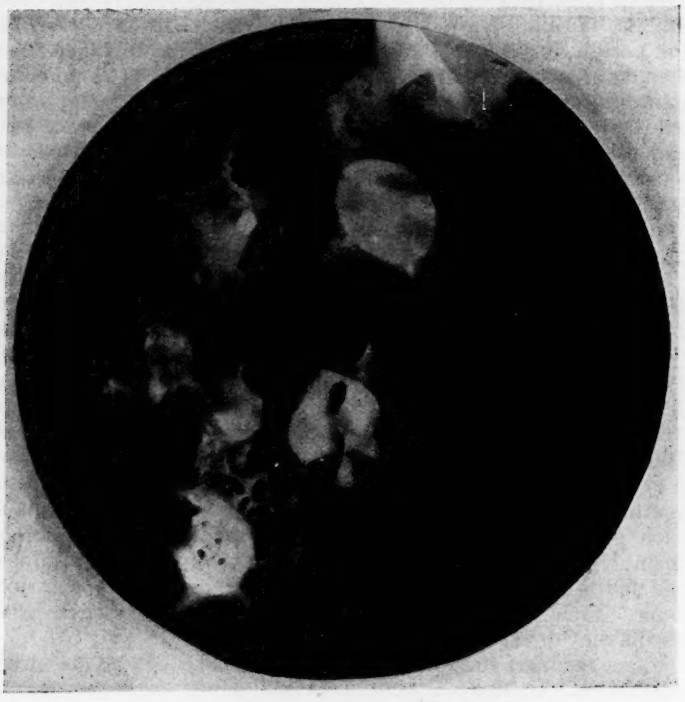
in many cases. There were obvious inclusion bodies rounded and sharply defined, large and small, both nuclear and cytoplasmic, more suggestive perhaps, morphologically, of Negri bodies, or the inclusions of variola, than of other varieties of cell inclusions. Some of these took up the red, others remained densely blue-black with the haematoxylin, still others showed a darker centre and pink periphery. I had previously observed similar staining effects when doing an experimental study of Negri bodies. The difference in staining reactions between the bodies in the same preparations could hardly be explained altogether by considering that the basic stain was removed from the periphery during differentiation, for, in the same field, one could see huge uniformly pink bodies and small blue-black bodies. In some cases, however, a grading off from the dense blue centre to a bright red periphery was very suggestive. As indicated, the bodies were of all sizes. Some were at least half the size of the cells, whilst others were minute, but definite. They were disposed in such numbers, and the cells had undergone such a considerable change at the points of invasion that it was difficult to trace the early stages. Outlying cells in some cases showed nuclear bodies, round and clear cut, without cytoplasmic bodies, and *vice versa*. It would serve no useful purpose here to go into the morphological variations, and there was insufficient material to attempt further methods of staining. It will be gathered that appearances differed very considerably from those seen in the rabbit's cornea in herpes febrilis, although perhaps too much stress should not be laid on differences in morphology, inasmuch as Negri bodies vary considerably in different animals. The distribution of the bodies may possibly be important as noted above. They are both nuclear and cytoplasmic, whereas in herpes febrilis they are said to be nuclear.

I was enabled through the kindness of Dr. Pandit and Mr. Hawley, of the King Institute of Preventive Medicine, to have microphotographs taken of some of the specimens, one of which is here reproduced.

There did not appear to be any leucocytes in the neighbourhood of the affected areas. Even had there been a slight leucocytic invasion superficial to Bowman's membrane, these cells might easily have been lost during the process of peeling off the epithelium, which also may be held responsible for excessive thinning out, or complete loss of the epithelial cells in some of the foci.

In addition to these inclusion bodies, another appearance was noted in five out of seven of the preparations of affected epithelium. In the superficial layers, both of the affected areas and elsewhere were larger or smaller patches of ill-defined, minute, ovoid or elongate particles. They were arranged, to a certain extent, in whorls. They lay on the superficial cells, and were traceable

between them. Near the thinned out areas, they were seen at a somewhat deeper level, but never in the cells. These may have been patches of invasion by small rod-shaped organisms. The concentric chain-like arrangement, which they sometimes formed,



Microphotograph of human corneal epithelium from a recent case of superficial punctate keratitis showing inclusion bodies (3rd day of disease). Haematoxylin and eosin.

suggested a growing colony. They were not sufficiently well-defined to photograph, nor were they seen at all in the Leishman or Giemsa preparations, but only in the haematoxylin preparations. I do not think they were artefacts, and Dr. Pandit concurred in this view. They may have been patches of some surface growth of an unfamiliar orgainsm. They had not been seen in any of the slide preparations so that, if present, the ordinary staining methods did not reveal them. One naturally thought that they might be concerned with the earlier phases of the corneal invasion, which subsequently produced the cellular degeneration, represented by fragmentation and formation of inclusion bodies.

With nothing further to go on other than these appearances, one could only speculate as to the nature of the objects. They gave the impression of being more definite and larger than the extracellular particles which have been discussed in connection with virus diseases.

Cocci and bacilli were seen here and there throughout both the normal and diseased epithelial preparations in all of the specimens.

The histopathological investigation was curtailed by lack of time and material. Clinical observations, animal experiments, etc., took up so much of our available time that histopathological material was stored in order to be worked out later. This was limited in amount and the opportunity was not forthcoming to augment it later on. For this reason the further investigation of these extracellular particles was not possible.

Experimental Production of the Disease in Man and Animals

At first an attempt was made to transmit the disease by direct transfer of epithelial scrapings taken as described above from the corneae of recently affected patients to the healthy corneal and other tissues of man and animals. Later on suspensions of more finely divided scrapings were filtered before attempting to infect the experimental animals in the following manner.

The epithelial débris collected from recent cases was finely divided up in a watch glass with a drop of saline and used to implant on the cornea or other part of the experimental animal. When the cornea was utilised as a site for transplantation it was cocainised and cleansed in the same way as the eye from which the material was taken. Corneae for implantation were usually traumatised, sometimes not. The trauma consisted in making one or more clean linear cuts with the sharp edge of a needle through the epithelium, impinging on, without actually cutting, Bowman's membrane. Epithelial pulp was transferred to the cornea thus prepared, and gently massaged in with the end of a smooth pipette, or rod. Sometimes this was repeated several times. When epithelial pulp was inoculated into the skin, the latter was prepared as for ordinary vaccination. Material from diseased corneae was usually obtained from several patients at the same sitting and mixed; sometimes, however, only one patient was available. We, fortunately, were able to secure a number of patients with suitable blind eyes, who allowed experimental inoculation and were agreeable to remain for a considerable time under observation. After the implantation, human eyes were covered with a wet pad and bandage till next day. Experimental eyes were subsequently subjected to routine examination with the corneal microscope. Cultures from the epithelial pulp were not made. Eyes from which

material was collected did not appear to be in any way adversely affected, and without exception they made an uneventful recovery with ordinary methods of treatment. When it was desired to filter the epithelial suspensions before transfer to the experimental animal, the technique was somewhat different. Several recently affected patients were chosen, three or more, and at one sitting material was collected as above, transferred to an agate mortar and broken up with sterile glass dust or sand, adding Locke's salt solution the while, to about 2-10 c.c. This suspension was then filtered through a Kitasato candle. A record of pressure was not kept in each case nor was a known organism mixed with the suspension to be filtered. The filters used allowed infective material to pass through under the conditions of the experiment, while under identical conditions, similar filters as tested at the King Institute, held back the pneumococcus and the B.influenzae. The filter candles used were Kitasato's porous tubes supplied by Messrs. Baird and Tatlock, London. This firm states that they are of German manufacture, the composition being about 80 per cent. Al_2O_3. The tubes are kilned at 1,450° C. and the porosity is about 0·7 μ. Three were new, *i.e.*, those used on November 28, 1928, December 11, 1928, and January 18, 1929. These small candles were selected on account of the scantiness of the volume of the suspension. The time and pressure, when available, is quoted for each experiment. In some cases cultures were made from the filtrate, and the filtrate examined for organisms under the microscope. The filtrate was used immediately for inoculation except in the last experiment.

Tables showing the details of the various animal experiments are appended. The positive findings may be referred to briefly here.

In experimental Group I, out of seven rabbits (five white, two black) inoculated on the cornea with unfiltered material, one developed superficial punctate keratitis. This was a black rabbit (No. 9). The eye showed no change for five days. On the sixth day, three discrete grey points appeared along the line of the needle scratch in the epithelium. They were slightly raised in the zone of specular reflection. Several other spots appeared after some days along the line, and an outlying point a short distance away. Some of these spots disappeared, but two of those along the line increased in size and became macular in type. The outlying spot became annular. The progress of the spots was very like that seen in the diseased human eye. At about the sixth week they resembled some of the types of macular keratitis very closely. There were, however, no pigmentary deposits or foldings of Descemet's membrane. Eventually on January 1, 1929, two months after inoculation, the three persistent spots had thinned out.

The left cornea of this animal was implanted with a large dose of unfiltered material with negative result.

In experimental group VI, out of seven cases in which unfiltered material was implanted on the human cornea three gave a positive result.

In the first case (woman No. 7) fine points appeared along the line of the scratch on the fourth day. By the ninth day the spots along the line were more numerous, and two outlying points some distance from the scratch were seen. These were rounded and slightly elevated and in one case a small dark centre developed (small ring form). About the twelth day there was a very definite extension of the process and the upper part of the cornea became covered with spots. Some ring forms were observed. The opacities still continued and were diffuse till December 5, 1928, when the patient desired to leave the city.

In the second case, a man (No. 8), curdy superficial opacities, and a few discrete spots, appeared on the ninth day. Two days later there was a very definite crop all round the lower half of the vertical scratch in the cornea. Some of these spots ran together to form a larger opacity in a way which suggested the branching of a dendritic ulcer when seen by retro-illumination, but they did not stain. He was kept under observation for six weeks. Most of the smaller spots had gone by this time, but the larger group was still visible although thinning out. There were pigmented deposits on Descemet's membrane.

In the third case, that of a man (No. 10), a series of very definite spots appeared on the sixth day. Two linear scratches at right angles had been made in the epithelium. By the eleventh day there were numerous opacities all over the cornea, for the most part to the nasal side of the vertical scratch. Two larger spots developed in the superior and inferior nasal quadrants. They were of the solid macular type. The patient could only be kept under observation for a month.

Transmission from the second filtrate (Group VIII) gave two positive results. Only two cases were done, a man and a woman. In the case of the man (No. 14), the corneal changes started on the fourth day. Definite punctate spots were present on the sixth day. There were pigmented deposits on the endothelium. The crossed scratches on the cornea showed a number of grey foci and there were also discrete outlying spots. In the case of the woman (No. 15), the cornea was traumatised by two small cross cuts. She could not be examined with the corneal microscope till the thirty-first day on account of an attack of dysentery for which she was sent to another hospital. By that time there were a number of macular spots independent of the scratches.

The third filtrate was only used for implantation on a single eye,

that of a man (No. 16). Crossed scratches were made on the cornea. For some time, only points of opacity along the lines of the scratches were noted. On the thirteenth day there were outlying spots near the upper limb of the vertical line. After a month another isolated spot was seen. This was not considered to be a typical case.

The fourth filtrate (Group X) used for four human eyes and one black rabbit gave a definitely positive result on the cornea of a woman (No 9), and a doubtful result on a man (No. 17). In the case of the woman, her right cornea had previously failed to take with unfiltered material and after fourteen days her left cornea was traumatised with crossed scratches and filtered material was implanted. On the third day, several grey foci appeared on the scratch lines. On the eighth day there were outlying spots. Some of the opacities were vesicular. In the case of the man (No 17), a single macular spot developed on the third day, annular in type. It was more definite three days later, but no fresh spots had appeared. There were no foci along the scratch lines. The patient had to be transferred to another hospital and was lost sight of.

Summary

The transfer of unfiltered epithelial suspension from a cornea affected by typical superficial punctate keratitis direct to the abraded cornea of a black rabbit reproduced the typical disease on the sixth day, as verified with the corneal microscope. It was only possible to obtain two black rabbits for this experiment. The second did not take the disease. In the case of seven white rabbits, the attempt was unsuccessful. Direct transfer of unfiltered material to the human cornea reproduced the disease in three out of seven. In one of these, the disease appeared on the third day. Under similar conditions the disease was not reproduced in the case of thirteen monkeys (M.sinecus). Attempts were made with unfiltered material to implant the disease on the skin of man, rabbits, calves, on the testicle of the rabbit, and on the brain by subdural inoculation in rabbits, but these were negative in so far as they went. Reproduction of the disease with filtered material implanted on the cornea was effected in the case of man in five cases out of eleven. Similar experiments failed in the case of seven white rabbits, three black rabbits and two monkeys. The earliest appearance of the corneal lesions was the third day. Apparently the disease is transmissible to man and black rabbits by corneal implantation. M.sinecus does not appear to be susceptible; possibly this is also the case with white rabbits. The animal experiments support the bacteriological and histopathological findings and the clinical features of the disease, and point to the aetiological agent being a specific filter-passing virus.

EXPERIMENTAL TRANSMISSION WITH UNFILTERED EPITHELIAL PULP

Experiments are arranged in groups, according to the type of animal used and the site selected for implantation, not in the order in which epithelial scrapings were taken and used for individual transmissions.

GROUP I.

Corneal Implantation—Rabbits.

Unfiltered material.

Animal	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Rabbit, white	1	16/8/28	Cornea R	Trauma with needle	Corneal microscope for 3 wks.	Negative
			do. L.	Without trauma	do.	do.
Rabbit, white	2	do.	do. R.	Trauma with needle (single scratch)	do.	do
			do. L.	Without trauma	do.	do.
Rabbit, black	9	30/10/28	do. R.	Trauma with needle (single scratch)	do. 2 months	Positive. Developed punctate keratitis on 6th day
Rabbit, white	10	do.	do. R	do.	do. 3 weeks	Negative
Rabbit, white	11	do.	do. R.	do.	do.	do.
Rabbit, white	12	do.	do. R.	do.	do.	do.
Rabbit, black	15	27/11/28	do. R.	Trauma with needle(crossed scratches)	do. 6 weeks	do.
Rabbit, black	9	18/1/29	do. L.	Linear trauma with needle	do. 1 month	do. R.E. of this rabbit had taken, see above

GROUP II.

Sub-dural Inoculation—Rabbits.

Unfiltered material.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Rabbit, white	3	16/8/28	Sub-dural	About 0·25 c.c. inoculated subdurally through drill hole	Animal kept under observation for 3 weeks	Negative
Rabbit, white	4	do.	do.	do.	do.	do.

GROUP III.

Vaccination on skin—Man, calves, rabbits.

Unfiltered material.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Rabbit, white	5	1/9/28	Skin, inner side of leg	Vaccination	Animal kept under observation for 3 weeks	Negative
Calf*	1	do.	Belly	do.	do.	do.
Calf*	2	do.	do.	do.	do.	do.
Man	1	do.	Forearm	do.	do. 2 weeks	do.
Man	2	20/10/28	do.	do.	do.	do.
Man	3	do.	do.	do.	do.	do.

*Carried out by Mr. Theodore at the King Institute, Guindy, vaccine depot.

GROUP IV.

Intra-testicular injection—Rabbits.

Unfiltered material.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Rabbit, white	6	27/10/28	Testicle R.	Injected 0·25 c.c. epithelial suspension	Observed daily for 6 weeks	Negative
Rabbit, white	7	do.	do.	do.	do.	Testicle removed sixth day and testicular emulsion inoculated subdurally into rabbits Nos. 13 and 14
Rabbit, white	8	30/10/28	do.	do.	do.	Negative
Rabbit, white & brown	13	4/11/28	Sub-dural	Emulsion of testicle of rabbit No. 7 0·25 c.c. injected subdurally	Observed daily	On 17/11/28 developed vesicular eruption on back. Died 14/12/28. Brain removed and emulsified. Emulsion inoculated subdurally to rabbit No. 16
Rabbit, white	14	do.	do.	do.	do.	Negative
Rabbit, white	16	17/12/28	do.	Emulsion of No. 14 brain (kept in ice 3 days) 0·25 c.c. injected subdurally	Observed daily for 3 weeks	do.

GROUP V.

Corneal implantation—Monkeys (M. sinecus).

Unfiltered material.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Monkey (M. sinecus)	1	7/11/28	Cornea R.	Linear trauma with needle	Corneal microscope 1 month	Negative
Do.	2	do.	do.	do.	do.	do.
Do.	3	do.	do.	do.	Naked eye and loupe 1 month	do.
Do.	4	do.	do.	do.	do.	do
Do.	5	do.	do.	do.	do.	do.
Do.	6	do.	do.	do.	do.	do.
Do.	7	do.	do.	do.	do.	do.
Do.	8	do.	do.	do.	do.	do.
Do.	9	do.	do.	do.	do.	do.
Do.	10	do.	do.	do.	do.	do.
Do.	11	do.	do.	do.	do.	do.
Do.	12	do.	do.	do.	do.	do.
Do.	13	do.	do.	do.	do.	do

All the monkeys were supplied by the King Institute of Preventive Medicine, Guindy.

Nos. 1 and 2 were sufficiently tame to retain in hospital for daily corneal microscope observations.

The remainder were retained at the Institute.

EXPERIMENTAL TRANSMISSION WITH FILTERED EPITHELIAL PULP.

Arranged in experimental groups in each of which the same filtered material was used.

GROUP VI.

Corneal implantations—Human eye.

Unfiltered material.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Man	4	8/11/28	Cornea	Linear trauma with needle (single scratch)	Corneal microscope daily, 1 month	Negative
Woman	5	do.	do.	do.	do.	do.
Woman	6	do.	do.	do.	do.	do.
Woman	7	15/11/28	do.	do.	do. 6 weeks	Positive 3rd day
Man	8	27/11/28	do.	do.	do.	Positive 9th day
Woman	9	28/11/28	do.	do.	do. 2 weeks	Negative*
Man	10	8/12/28	do.	do. (crossed scratches)	do. 4 weeks	Positive 6th day

*Subsequently inoculated with filtered emulsion and gave a positive result.

GROUP VII.

First filtrate.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation	Observation.	Result.
Rabbit, black	17	28/11/28	Cornea R.	Linear trauma	Corneal microscope 6 weeks	Negative
Rabbit, white	18	do.	do.	do.	do.	do.
Woman	11	do.	do.	do.	do.	do.
Rabbit	19	do,	Testicle	Injection	do. till 7th day	On the 7th day testicle removed and emulsified in sterile glycerine, kept on ice for 10 days and implanted on human corneae Nos. 12 and 13
Man	12	15/12/28	Cornea R.	Linear trauma	do. 4 weeks	Negative
Man	13	do.	do.	do.	do.	do.

New Kitasato filter candle used saturated wi. Locke's solution and autoclaved.
The volume of the suspension made up from 3 cases was 10 c.c.
Time of filtration 30 minutes.
Pressure not recorded.
Cultures from filtrate not made.

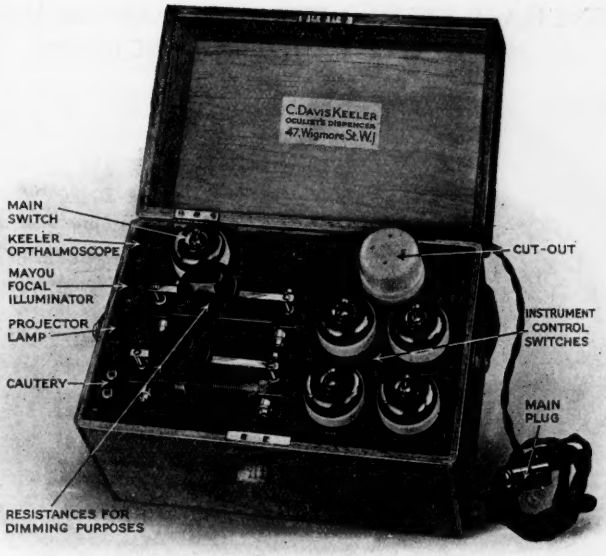
GROUP VIII.

Second filtrate.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Man	14	1/12/28	Cornea R.	Linear trauma	Corneal microscope 1 month	Positive 4th day
Woman	15	do.	do.	do.	do.	Positive, day not noted, patient ill with dysentery. First seen on 31st day

Previously used filter employed.
Saturated with saline and autoclaved.
Volume of suspension from 4 cases 3 c.c.
Time of filtration 45 minutes.
Pressure not recorded.
Cultures from filtrate not made.

A Keeler Portable Resistance Equipment



THE illustration presents the new equipment for supplying the instrument as enumerated above from high voltage house supply.

For further particulars apply to

C. DAVIS KEELER,

Oculists' Dispenser and Scientific Instrument Manufacturer,

47, WIGMORE STREET, LONDON, W.1

BRANCHES—PLYMOUTH, TRURO and PENZANCE.

CLEMENT CLARKE, LTD.,

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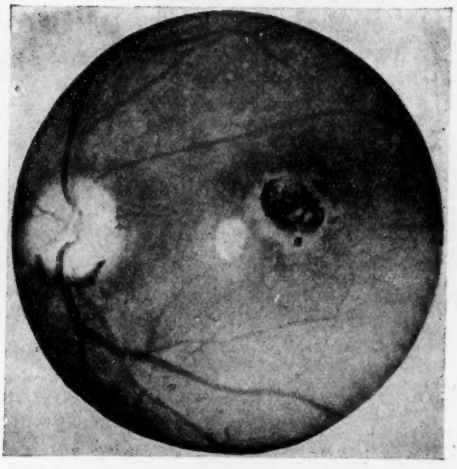
FINCHAM STEREO-FIXATION APPARATUS USED WITH BJERRUM SCREEN

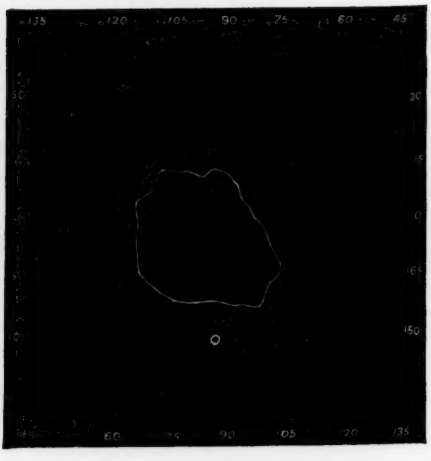


Reversed and inverted photograph of an old case of macular atrophy for comparison with campimetry record.

White spot at centre is due to reflex in instrument.

(Photograph by courtesy of Messrs. Curry & Paxton.)

The irregular white line is the map of a scotoma which was recently recorded on the Fincham apparatus in the above case. The small spot below the central area is caused by a spot of pigment immediately above the macula. The test object employed was a 1 mm. disc at a distance of one metre. The radii of the circles of the chart subtend at the eye the angles of 1, 2, 4 and 6 degrees respectively.



GROUP IX.

Third filtrate.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Man	16	4/12/48	Cornea R.	Linear trauma	Corneal microscope 1 month	Positive

Previously used filter employed.
Prepared as before.
Volume of suspension from 7 cases 4 c.c.
Time of filtration half-an-hour.
Cultures of filtrate not made.

GROUP X.

Fourth filtrate.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Woman	9	11-12-28	Cornea R.	Linear trauma	Corneal microscope 1 month	Positive 3rd day
Man	17	do.	do.	do.	do.	Positive (?) Only one annular spot observed 3rd day. Patient transferred to another hospital 6th day
Man	18	do.	do.	do.	do.	Negative
Man	19	do.	do.	do.	do	do.
Rabbit, black	15	do.	Cornea L.	do.	do.	do. Had failed to infect this animal's R. E. with unfiltered material

New filter used.
Saturated with Locke's solution and autoclaved.
Volume of suspension from 5 cases 10 c.c.
Filtered in 20 minutes at a negative pressure of 25 cm.
Cultures from filtrate showed contamination as also did controls.

GROUP XI.

Fifth filtrate.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Man	20	18/1/29	Cornea R	Linear trauma	Corneal microscope 1 month	Negative
Rabbit, white	20	do.	do.	do.	do.	do.
Rabbit	17	do.	do. L.	do.	do.	do.

New filter used.
Prepared as before.
Volume of suspension from 4 cases 10 c.c.
Filtered in 15 minutes at 20 cm.
Cultures from filtrate negative.

GROUP XII.

Sixth filtrate.

Epithelial scrapings on different dates (March 16, 18, 20 22 and 25, 1929). Stored on ice at the King Institute and filtration carried out there.

Animal.	No.	Date.	Site of Inoculation.	Nature of Inoculation.	Observation.	Result.
Man	21	8/4/29	Cornea L.	Linear trauma	Corneal microscope 1 month	Negative
Woman	22	do.	do.	do.	do.	do.
Rabbit, black	21*	do.	do.	do.	do.	do.
Rabbit, black	22*	do.	do.	do.	do.	do.
Rabbit, black	23*	do.	do.	do.	do.	do.
Monkey	14	do.	do.	do.	do.	do.
Monkey	15	do.	do.	do.	do.	do.

*Very young, bred by No. 15 of a white doe in the hospital laboratory, as it was found so difficult to obtain black rabbits.
New filter used.
Prepared as before.
Volume of suspension 1½ c.c.
Filtered in 10 minutes at 25 cm.
Cultures from filtrate negative.

The bulk of the work in connection with this investigation was carried out in the various departments of the hospital with the help and co-operation of the members of my staff. Dr. K. Koman Nayar (Assistant Superintendent), besides giving much other valuable assistance, took over the corneal microscope observations during my absences. Messrs. Venkatarangam Naidu, Narayanaswami Pillai, Narayanaswami Naidu, Narayana Iyer, and the late Dr. V. G. Muthayya, observed and made appropriate notes on the cases as they came under their departmental supervision. Mr. Narayanaswami Pillai, however, undertook the most laborious share in this combined effort, inasmuch as he was responsible for maintaining records of the individual cases, including the notes on biomicroscopical findings, selection of cases for experimental work, and all our hospital laboratory routine and animal work. Lt.-Col. H. H. King, I.M.S., Director of the King Institute of Preventive Medicine, Guindy, kindly gave his help and advice. He allowed Mr. Theodore of his staff to visit the hospital frequently and co-operate with us in connection with the laboratory investigations. In this way we were enabled to keep in touch with the King Institute, which is situated seven miles away. Col. King supplied some of the rabbits, all of the monkeys and also the culture media and apparatus in connection with the filtration experiments. Mr. Theodore carried out a large portion of the animal experiments in groups 3, 4, 5 and 12 and attended the hospital on numbers of occasions with all the necessary materials and apparatus to help in cultural and filtration work. Dr. Pandit, Assistant Director of the King Institute, Guindy, and Mr. Hawley of the Institute staff also lent their aid. To all these gentlemen my grateful acknowledgements are due.

TWO CASES OF SYMPATHETIC OPHTHALMITIS

BY

D. J. WOOD

CAPE TOWN

WITHIN the last year I have had two cases of sympathetic disease which, taken with the case described by me in this journal in May, 1927, form an interesting trio.

The 1927 case (R. W.), one of gross disease of the choroid and iris in the exciting eye, followed by a serious infection of the sympathising eye, was unusual in the complete recovery which the sympathising eye made, so that to-day it possesses 6/4 vision with scarcely a trace to tell the tale of what it had gone through.

My third case is even more unusual as the sympathetic disease occurred after a successful operation for cataract where there were no symptoms to warn one of danger, and where the patient got, and still has, standard vision in the exciting eye.

The second case of the trio was a coloured boy (E. B.), who was wounded by a piece of wire in a fight. He had a wound of the upper corneal margin with prolapse of the iris. The prolapse was cut off next day, and a small conjunctival flap drawn over the wound. No redness or pain followed, but after two weeks the iris had changed its colour, was pushed forwards, and the tension had gone down. There were no deposits on the cornea. The eye was excised three weeks after the injury, and the boy left.

He was brought back in two weeks with failure of vision in the remaining eye. There was little redness, but definite deposits on the back of the cornea, and some adhesions of the iris. From that time there elapsed nearly a year, during which he had a long course of neo-salvarsan, sodium salicylate, mercury, and recently hexamine. None seemed to make any difference. There is still much " K.P.", little redness, but almost complete adhesion of the iris to the lens, and much deposit on the lens capsule. While one could still see into his eye there was congestion of the retinal vessels and loss of outline of the optic nerve. Microscopic examination of the exciting eye was rather surprising, as the dominant feature was a leucocytic extravasation, with few collections of lymphocytes, and very few plasma cells.

A few points may be mentioned by way of contrast to the next case.

Except at the wound the cornea was normal, but on Descemet's membrane there were clumps of polymorphonuclear leucocytes. The angle of the anterior chamber was full of them, as was the coagulum in the Chamber. (Fig. 1.) They were in large numbers in the iris, but it retained its proper tissue elements, and bleached sections (Fig. 2) showed that the uveal pigment cells, though irregular in size and arrangement, were present practically all along the back of the iris. At the pupillary region there was a definite lymphocyte collection. The frequency of these collections has probably a relation to the vicinity of the circulus minor. They are seen in many cases of continued iritis. The ciliary body on the side of the wound showed the ordinary changes seen in traumatic cyclitis, plus a rather large lymphocyte collection just below the surface, elsewhere the changes resembled those in the iris.

The retina had suffered more than one would have expected, the damage starting apparently from the inner surface. (Fig. 3.) The nerve fibre and ganglion cell layers were destroyed, and leucocytes were in large numbers as far back as the rods and cones. The optic nerve was normal. Except for the few collections of lympho-

cytes the condition was not typical of sympathetic disease, but nevertheless it produced in the other eye a condition which was quite typical.

The third case of the trio (Mrs. M.), came to me in December, 1927, with commencing cataract. She was a woman aged 53 years, and had been injured in the left eye when a girl. She was treated by Sir George Berry, and had all her life a small cystoid cicatrix with an updrawn pupil. It had never given any trouble, and, till her sight failed as a result of cataract, she had never been incommoded by the little damage. I put her off for six months, but by that time she saw too ill for her household duties, and as the left lens was more opaque, I removed it on June 14, 1928. The operation was normal. No iridectomy was needed, and she would have been discharged in two weeks had she not given herself a corneal abrasion. Examination of the eye on account of this revealed about half a dozen spots on the back of the cornea, which, however, were very transitory. On August 7 I did her a discission of the lens capsule, and she got 6/6 vision which she still has. She left with no visible abnormality save the updrawn pupil, perhaps a little more eccentric than at first.

She returned on September 1 with iridocyclitis in her right eye, precipitates on her cornea, redness and dim vision. As sympathetic disease seemed unthinkable, a careful examination was made, but nothing was found save one doubtful tooth which was removed. She grew steadily worse, her pupil keeping small, the precipitates increasing, and the eye looking like a sympathetic case. Her left eye was absolutely free from any suggestion of inflammatory mischief. (Slit-lamp examination.)

She went away for a change and was absent for some months, but returned much worse, with severe pain, and no perception of light. I advised the removal of the eye, and she gladly agreed. It was removed on March 21, 1929. This was nearly nine months after the operation for cataract, and much longer therefore than would have been the case had one had to remove an exciting eye. Also as there had been no wound in the sympathising eye, one had to do with the effects of uncomplicated sympathetic disease. The eye on section showed the vitreous coagulated, and the retina in place. It was embedded in celloidin, cut, and stained in various ways. Heidenhain's iron-alum-haematoxylin gave the best results in the way of detail. The bacillary layer of the retina was only slightly abnormal, but every other portion of the eye was more or less damaged by infiltration or destruction, and the predominating feature was the presence everywhere of vast numbers of plasma cells. These stained better with Heidenhain's method than by any other tried, their chromatin marking in the nucleus being very striking, and unmistakable. Lymphocytes stained deep blue or

black, while the nuclei of endothelial cells stained only a faint blue. All three are therefore easily and certainly observed.

It was found that, except in the iris, plasma cells and lymphocytes were fairly sharply separated. Lymphocyte nodules, where they occurred, were bordered by plasma cells, not mixed with them. In the retina larger vessels had a coating of lymphocytes, while small ones had a layer of plasma cells round them. A mixture of the two kinds of cells such as was found in my 1927 case did not occur. Endothelial nuclei were found nearly everywhere, but not in collections, and giant cells were not found anywhere except in the cell exudate in front of the optic papilla, a situation where one would not have expected to find them.

Taking the tissues from before backwards, one found that the corneal epithelium was unaltered save for intrusive lymphocytes in small numbers which had penetrated Bowman's membrane. Beneath this, all round the corneal margin, was a zone of lymphocytes bordered by plasma cells, with increase of the corneal cells proper. This had been invisible during life, showing a greater transparency to have been present than is usually the case with corneal exudates. At the margin of the plasma cell exudate there were cells showing intermediate changes. Some nuclei showed multiple nucleoli, in others the chromatin was broken into masses, while others showed the characters of the plasma cell but in a nucleus still oval. A similar process could be seen in the cells of the tissue filling the anterior chamber, and also in the iris proper. Descemet's membrane appeared normal, and one could trace its endothelium nearly everywhere, but as the anterior chamber was full of new-formed tissue there was a doubt whether it was derived from the iris or possibly from the corneal endothelium. The former is, however, much the more probable. The cells in the anterior chamber were very definitely in layers (Figs. 4, 5, 6) and the nuclei, though mostly long ovals, all showed the plasma cell facies in their chromatin marking.

There was a definite separation line between these cells and the plasma cell collection which represented the iris. During life they were sufficiently transparent to give the impression that there was a shallow anterior chamber.

The iris has been changed into a mass of closely packed plasma cells, with some scattered lymphocytes and endothelial cells. (Fig. 4.)

The blood vessels have undergone hyaline degeneration (Figs. 7 and 8). No muscular coat is visible, and the adventitia is thickened, transparent, and devoid of the normal finely fibrillar structure. It gives the staining reactions characteristic of early hyaline change, taking a pink with eosin and a fairly bright red with van Giesen's stain. Hyaline degeneration is indicative of

FIG. 1.

E.B. Angle of anterior chamber and iris, both full of leucocytes, which are also seen on surface of iris and back of cornea. Pigment layer not destroyed. ×70

FIG. 2.

E.B. Iris bleached to show cells of pigment layers. Dilatator pupillae can be seen lying beneath them. ×140

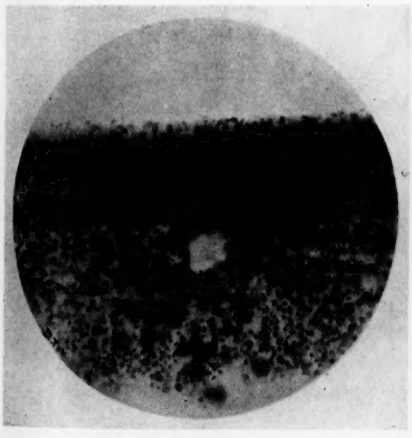


FIG. 3.

E.B. Retina invaded by leucocytes, nerve fibre and ganglion cells destroyed. ×140

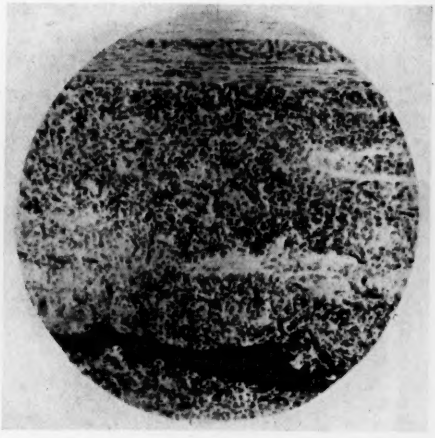


FIG. 4.

Mrs. M. Iris changed into mass of plasma cells. Filling anterior chamber re layers of cells whose nuclei show plasma cell marking Iris contains remains of extra-cellular pigment, and vessels formed by endothelium only. Behind the irregular line of pigment are more plasma cells, cells from the ciliary epithelium and broken down nuclei. ×140

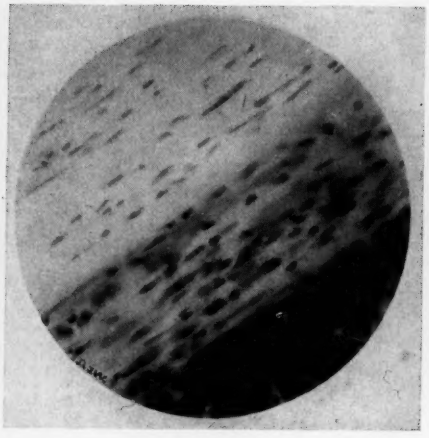


FIG. 5.

Mrs. M. Cells between cornea and iris. ×280

FIG. 6.

Mrs. M. The same under higher power to show the plasma cell marking. ×560

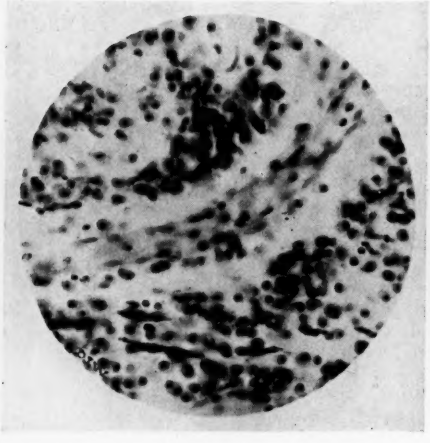


FIG. 7.

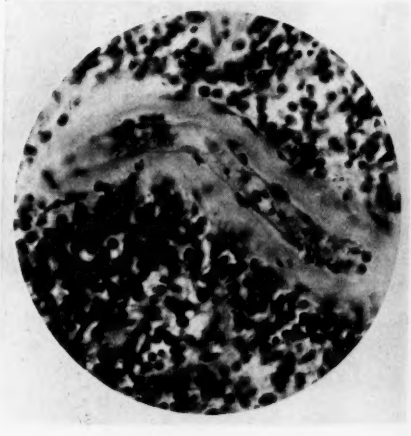


FIG. 8.

Mrs. M. Vessels in iris showing hyaline material round an endothelial tube. Most, if not all of the cells showing in the hyaline substance are in front of, or behind it. Endo- or perithelial cells border the hyaline exudate. ×280

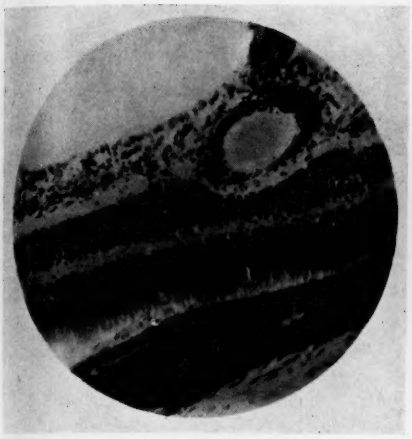


FIG. 9.

Mrs. M. Retina. Inner layers full of plasma cells. A large vessel with its sheath of lymphocytes. ×140

FIG. 10.

Mrs. M. Lymphocytes which have penetrated membrana limitans interna and entered vitreous. ×140

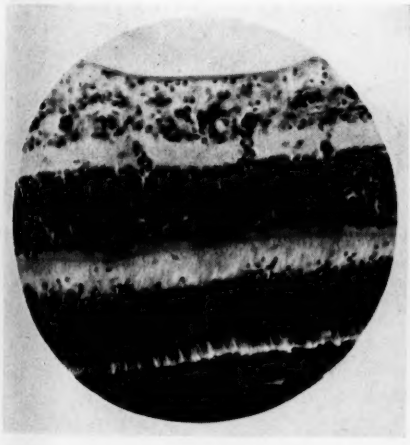


FIG. 11.

Mrs. M. Nerve fibre and ganglion cell layers showing plasma cells covering small vessels lying parallel to the surface and sending smaller branches into the bipolar cells.

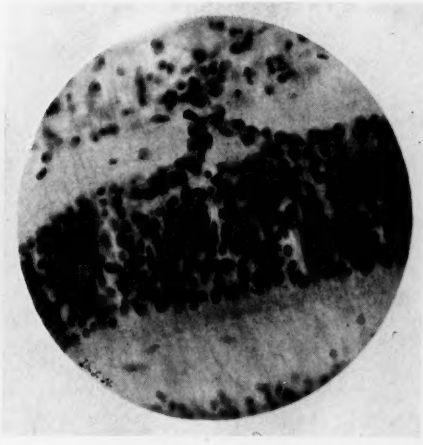


FIG. 12.

Mrs. M. Detail of same. ×480

acute infective processes, and is not infrequently found in eyes excised for iridocyclitis. The endothelium appears unaltered. Some vessels contain blood, others are empty. Few, however, seem to be normal in the amount of blood present, and in a good many the blood cells are only ghosts, hardly staining with eosin.

The hyaline tubes are surrounded with endothelial or perithelial cells, and are sharply separated from the plasma cells round about. The hyaline matter is so transparent that only careful focusing shows that plasma cells are in front of or behind and not in the hyaline matter. In several sections one could see that endothelial cells near the blood vessels showed a plasma cell marking in their chromatin.

Everywhere one could see plasma cells which contained two nuclei, and with a cell body a third bigger than normal. In spite, however, of many hours spent in examining sections I found only one instance of mitosis in what seemed to be a plasma cell. The chromosomes were arranged at the two poles of an elliptical nucleus in an oval cell staining in the same way as surrounding plasma cells. Either the plasma cell is an end product, or it is very stable and the act of mitosis occurs quickly. Otherwise one would have found more examples.

A good many plasma cells could be found degenerated, the cytoplasm being either granular or unstained, and with the definite chromatin marking blurred.

Pigment granules were found all through the iris, and one noticed the same peculiarity seen in my first case (R. W.), that the pigment particles floated up in the mounting medium and lay close to the cover glass.

About two thirds back from the surface of the iris (Fig. 4) there was an irregular layer of pigment, and behind it was a band of broken up cells, apparently derived from the ciliary epithelium, which extended forwards into the pupil. Bleached specimens showed that the pigment was all extra-cellular. There were no traces of the columnar cells which form a striking part of normal sections.

The sphincter muscle could be traced as a pale band, but the cells were swollen and stained ill. There was of course no trace of the dilatator.

Over much of the ciliary body one could see in bleached sections both layers of the epithelium, but over the plane part there was more destruction reaching backwards to a thickened ora serrata. From this region much exudate had passed on to and around the periphery of the lens, but the cells were all broken up. The lens capsule had given way and lymphocytes and mononuclear cells could be seen inside it.

The choroid near the ciliary body contained some lymphocyte

collections but further back was normal. The retina was in place, but showed numerous changes, probably more fundamental than the microscopic appearances suggested as the eye was blind. The larger vessels had sheaths of lymphocytes (Fig. 9), and these cells had penetrated in many places into the vitreous (Fig. 10). Elsewhere in the retina they were few. Plasma cells were numerous. They lay in a regular layer along the membrana limitans interna which seemed abnormally thick, their nuclei were all next to the membrana, nowhere had they penetrated it, and none were to be seen in the vitreous. The small vessels of the retina were all covered by a coating of plasma cells (Figs. 11, 12), and one could not see the vessel walls except in section. Most of these vessels lay parallel to the surface, but they gave off branches which one could follow by means of the plasma cells on them, and which passed deeply as far back as the back of the layer of bipolar cells. No plasma cells could be found deeper than this layer. This agrees of course with the normal blood vessel distribution. The outer layers of the retina seemed to be normal, but near the optic nerve Heidenhain's stain showed a number of the cone nuclei stained an intense black. This appeared in all sections.

In front of the optic nerve there was a collection of cells of many kinds evidently derived from the papilla, lymphocytes, plasma cells, endothelial cells, and a few giant cells with many oval nuclei staining ill. The central vessels of the nerve had lymphocyte sheaths and there were lymphocytes in the position of the lamina cribrosa.

All through the eye the separation of lymphocytes from plasma cells was noticeable, and suggestive of different origins. The plasma cell marking in nuclei, which were still elongated and which seemed to have intermediates between them and endothelial cells, further indicates an origin from the latter as found on the outside of blood vessels. The stationary character of the plasma cells is shown by their failure to pass the membrana limitans interna, and their relative fewness inside the blood vessel tubes. They are, however, the outstanding feature in the histology of the case, and are in infinitely greater numbers than either lymphocytes or endothelial cells. One gets the impression that they are the response to a toxin, but not to that of ordinary sepsis, since there was not a single leucocyte to be found anywhere outside the blood vessels, and few even in them.

One may notice that Heidenhain's stain will stain microbes black if the staining process be long continued, but no evidence of bacteria could be found anywhere.

It is interesting to note that though the retinal changes were not excessive, the eye was blind. I have seen the same result in the eye of a leper. In it the retina appeared to be quite normal, and all

changes to be confined to the anterior segment of the eye. Possibly special methods of staining might show degeneration of the ganglion cells.

The two cases are apparently the two extremes of what we know as sympathetic disease. In one the inflammation is of the septic type, characterised by leucocytic extravasation, and some lymphocyte collections, in the other by the absence of leucocytes, but with some lymphatic collections and with much plasma cell formation. The common type shows mainly lymphocyte nodules.

One would hope that the third case is unique. To find destructive sympathetic disease following a successful operation for cataract, where the only evidence of inflammation was the presence of a few precipitates on Descemet's membrane which were visible for a few weeks at most is fortunately unusual.

It is, however, evident from the case E. B., where a possibly dangerous eye was removed, that one does not do all that is necessary unless one makes a careful slit-lamp examination of the remaining eye before the case leaves hospital, and again afterwards till safety is assured. The same would hold good for any post-operative evidence, however slight, if iridocyclitis is present, though in a case like my last it is difficult to see what one could have done to prevent trouble, in the face of the fact that the exciting eye was and is free from disease.

AN UNUSUAL CASE OF NEURO-EPITHELIOMA OF THE RETINA

BY

D. G. PATWARDHAN, D.O.(Oxon.), D.O.M.S.(Lond.), M.B., B.S.(Bomb.)

OPHTHALMOLOGIST, B.J. MEDICAL SCHOOL

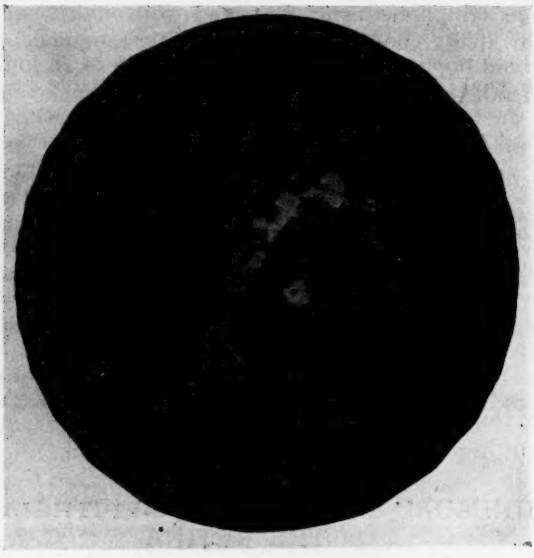
POONA

THE patient, a boy aged 6 years, was brought to Poona, Sassoon Hospital, and was admitted for treatment on June 25, 1929.

State on admission.—The patient had a tumour of the left eyeball of the size of a coconut and he complained of extreme pain in that region. He was not emaciated and the state of his health appeared to be fairly normal.

History of the case.—About six months previously the patient had an injury to the left eyeball. The eyeball was perforated and there was a good deal of haemorrhage. There was no help available from a doctor and hence he was treated by homely

remedies. The bleeding stopped and the wound healed for all practical purposes. The patient lost his eyesight. After about a week or so there appeared a swelling at the site of the injury of the size of a ground-nut. This swelling went on increasing gradually until it attained its present size. All sorts of medicines were tried



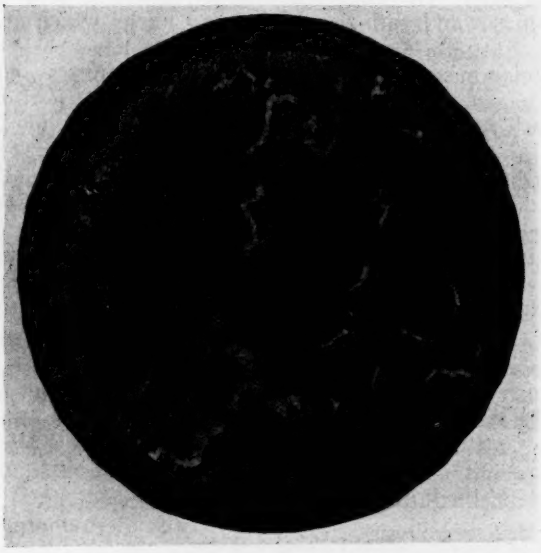
Photograph showing masses of cells surrounding lumina that do not contain any blood. They seem to represent badly formed rosettes found in tumours of slower growth.

without avail. The pain was increasing along with the increase in the size of the tumour.

On examination it was found that the swelling was as big as a coconut covering the area from the nose on the inner side to the tragus of the left ear on the outer side, and from about an inch above the orbital margin low down to the angle of the jaw. The actual measurements were from side to side 10 inches; from above downwards 9 inches. The circumference was 15 inches. The tumour had a stalk originating from in between the eyelids and it was not adherent to any of the surrounding structures. It had a very foul smell and its consistency was as soft as brain. The appearance was lobulated with depressions in between which were areas studded with yellowish looking material. In some places

bleeding points could be seen. There was no enlargement of the glands of the neck. The fundus of the other eye was perfectly normal and the media clear. The vision of the sound eye was 6/6.

X-ray Report.—No secondary deposits in the viscera were found. The X-ray photograph of the skull did not reveal any shadow.



Low power photograph showing the growing edge of the tumour, profuse haemorrhages present, cellular masses traversed by sinuses.

A photograph was taken from the front as well as sideways. The tumour was removed under chloroform on July 2, 1929, and exenteration of the left orbit was done. There was not much bleeding during the operation. The weight of the tumour was taken after its removal and was found to be 620 grammes. The tumour as well as the exenterated material was sent for the pathologist's report.

Clinical diagnosis.—Glioma (exophytum) of the retina.

Pathological findings.—To the naked eye the tumour is a fungating cauliflower-like mass, soft and somewhat elastic to the touch, with elevations and depressions on the surface which here and there shows signs of ulceration. There are clearly discernible

bleeding points on the surface and also sticky pus-like material, especially in the furrows. In size the tumour is larger than a fist and there is on the under surface the mark indicating the division of what looks like a pedicle.

Microscopically one can recognise areas of degeneration in the midst of fairly well preserved tissue which gets scantier towards the central portion of the growth, as judged from sections taken from this part. The undegenerated portions consist of cells poor in protoplasm and with deeply staining nuclei which are oval or rounded. Mitotic figures of various kinds have been observed. The cellular masses are traversed by blood sinuses and profuse haemorrhages are present. The degenerated portions show " ghosts " of cells with nuclei either entirely unstained or slightly so, being in places piknotic. Islets of fairly well preserved cells are discernible here and there in these areas, arranged around lumina that do not contain any blood. One fails to find regular " rosettes." There are here and there cells with large elongated ovoid faintly-staining nuclei with fibrils and here and there endothelial cells are present. In the neighbourhood of ulcerated areas polynuclear leucocytes are found penetrating the substance of the growth.

Diagnosis.—Neuro-epithelioma of the retina.

The only peculiarity in the case in point was the unusual size of the tumour and the short period during which it attained such a huge size. Similar cases are reported in " Surgical Pathology," by McFarland, and in Banerjee's " Text Book of Pathology."

I am indebted to Dr. Noronha, Pathologist, B. J. Medical School, for having kindly lent me two micro-photographs of sections of the tumour.

ANNOTATION

The other half of the Story

It was at one time the habit of a certain section of the legal community to concoct an apparently impossible story and demand some rational explanation of the sequence of events. The best known one, reputed to be true, concerns a girl and her mother who visited Paris at the time of the great exhibition. They had come from abroad and took rooms at an hotel where they had dinner together. Their rooms were next door to each other, and they retired to bed at about 10 o'clock in the evening. When the daughter awoke next morning she tried to go to her mother's room

to have early tea with her, but found the communicating door locked. She rang for the chambermaid who assured her that the room was untenanted; and, as the daughter did not believe this obtained a key and showed her the bed which apparently had not been slept in. The story can be lengthened to any degree by giving an account of the daughter's interviews with various people; the maitre d'hotel; the waiters; the cabman who drove her from the station; etc., all of whom gave the same reply, namely that she arrived alone at the hotel without her mother. The story has been used to test the ingenuity of many legal brains. It is thought that only one of these provided the rational and supposedly true explanation, namely that the mother did arrive with the daughter, but died in the night from plague which she had contracted while abroad. A case of plague in Paris at this time would have wrecked the prospects of the exhibition, so the body was removed secretly at night, and all who had seen the deceased lady during life were bribed not to admit it.

Though not requiring the same degree of ingenuity, the following three instances, related by Thomas Hall Shastid in the *American Journal of Ophthalmology* may prove interesting. The first concerns a presbyope who was seen by Shastid every 6 months for a " check up " of his refraction. He suffered from headaches after reading which completely disappeared for a short period after his check up, only to appear again later. A full general examination failed to disclose any cause for this anomalous state of affairs, which remained unexplained until the patient's wife was seen. Her words were " Well, you see, hubby at night is always very tired, or else lazy. So, after dinner he used to sit in the living room and go to reading with his distance glasses, his near glasses being upstairs, therefore too far away for him to get them. He always expected to read ' just for two or three minutes.' But always, of course, he would stick to the job for two or three hours. Next day he would have a frightful headache." After each check up, however, the man would be sufficiently interested in his eyes to get and use the near glasses for night reading, though after a few days he would fall into the old habit of using his distance glasses for this purpose. Needless to say a pair of bifocals cured him of headaches.

A second case was a man who already had bifocals but from time to time would suffer from severe headaches. He was a small man and his occupation necessitated frequent conversations with other men on the public streets. Being short he had to look through the upper, distance, portion of his glasses, and the strain of trying to see the facial expressions of his interlocutors at perhaps two feet, through distance glasses brought on headaches. In this case they were completely cured by provision of a pair of +1·25D. spheres

in a grab front to be worn whenever he was talking to men he could not look down on.

The third case was again a patient with bifocals who found her glasses excellent for distance but productive of much blurry vision when she looked through the lower segments for reading. Examination of her glasses showed that the temples were just a trifle loose so that she was frequently putting her fingers against the lower part of her lenses so as to push the glasses higher up her nose, thus fogging them. Tightening the temples effected an immediate cure. The patient, though a highly educated woman, had been unable to make this simple observation herself.

COUNCIL OF BRITISH OPHTHALMOLOGISTS

Annual Report

THE Council presents its report for the year 1929-30. At the first meeting the following were elected as officers:—President, Mr. J. Herbert Fisher; Vice-Presidents, Sir W. Tindall Lister, Sir J. Herbert Parsons; Hon. Treasurer, Mr. M. S. Mayou; Hon. Secretary, Mr. Frank Juler. The following were appointed to serve on the Executive Committee:—The President and Secretary (*ex officiis*) with Mr. Treacher Collins, Sir W. Lister, Sir J. H. Parsons, Messrs. Mayou, Goulden and Williamson-Noble.

Report on admissions to Ophthalmia Schools at White Oak, Swanley.—A deputation from the Council attended at the Ministry of Health with proposals to facilitate the admission of children from the extra-metropolitan areas into the schools. The obstacle to extending the use of the schools is financial, and little hope was held out by the representatives of the Minister that any assistance could be afforded by the Ministry. It was pointed out that the cost of maintenance per child would diminish if the number of children were increased. The Board of Education has been approached in regard to the advantages of specialist examination of children in extra-metropolitan schools, since the Council has reason to believe that a certain amount of ocular disease, which would benefit by residential treatment at Swanley, escapes detection.

Ophthalmic Benefit.—Since the last report, certain developments have taken place in the possible methods of administration of ophthalmic benefit, and at a joint meeting of the Executive Committees of the Council and the British Medical Association a prolonged discussion on policy took place. As a result the Association invited the Council to nominate three representatives to

serve on its Ophthalmic Committee. This the Council agreed to do, and Messrs. Fisher, Mayou and Juler were nominated for this duty. The British Medical Association has established a scheme of clinics on lines which are not universally approved, and other schemes are being actively discussed. The subject is receiving the constant attention of the Executive Committee.

Report on Ophthalmia Neonatorum.—Copies of this report have been circulated and brought to the notice of the County and Borough Authorities which deal with Maternity and Child Welfare.

Report on the "Refraction Hospitals."—This report has been received and is under consideration by the Executive Committee.

The Council desires to thank the Council of the Royal Society of Medicine for the use of rooms for meetings, and the National Committee for the Prevention of Blindness (U.S.A.) for continuing to send copies of its publications.

As in former years, the expenses of the Council have been defrayed by contributions from its members.

ABSTRACTS

I.—RETINA

(1) **Dubois, Hélène (Lausanne).—Traumatic detachment of the retina and operative treatment. (Décollements rétiniens traumatiques et traitement opératoire.** *Ann. d'Ocul.*, Vol. CLXV, p. 81, 1929.

(1) **Dubois** quotes the references to some of Gonin's writings from 1921 onwards in which complete and lasting recovery from retinal detachment is possible by operation (closure of holes in the retina). She points out that Gonin refers only once to detachments other than spontaneous. Traumatic detachments due to haemorrhage or oedema may be of better prognosis than spontaneous detachments, but detachments due to retinal tears from a violent concussion injury or to a cicatricial contraction after a penetrating injury are in a different category. Operation on a traumatic detachment with a hole in the retina is reported as having been successful after a single application of the thermocautery which produced closure of the rent. In this case there were no vitreous bands. Other cases are described, which were treated at the ophthalmic hospital in Lausanne, in which operation was not successful in restoring the retina completely to its position owing

to adhesions and cicatricial bands following penetrating wounds. The following conclusions are drawn:

(1) Traumatic detachments with retinal tears at the ora serrata are capable of rapid and complete recovery as in cases of spontaneous detachment.

(2) Traumatic detachments from cicatricial contraction, the result of minute foreign bodies are also of good prognosis.

(3) When the retinal holes are due to the traction of bands following penetration by a large foreign body or of penetration by a pointed instrument, recovery is unlikely.

HUMPHREY NEAME.

(2) **Lindner, K. (Vienna).—On the results obtained up to the present in the treatment of detached retina by Gonin's method. (Die bisherigen Behandlungserfolge der Netzhautabhebung mit dem Verfahren von Gonin).** *Wien. Klin. Wochenschr.*, Vol. XLIII, p. 225, 1930.

(2) **Lindner** reports on the results obtained in his clinic during 1929 by the use of Gonin's method of treatment of retinal detachment, which aims at curing the condition by sealing the hole in the retina by means of the cautery. In all 42 cases came under observation, in 29 of whom one or more holes could be seen; of these 29 only 25 came to operation, and Lindner reports cure for no less than 11, thus giving a percentage of 44. But actually the results that can be obtained are better, for out of 25 only 14 were recent cases, *i.e.*, of no more than six weeks' duration, and of these 14, no fewer than 9 were cured, a percentage of 64. The time factor is a most important condition of success, for cases of longer standing than six weeks give progressively poorer results; out of 7 cases, ranging in duration between six weeks and nine months, only two were cured, one case being of seven months' standing and the other of four. The remaining four cases in Lindner's series were of a duration ranging between one and six years; operation was a failure in all these four.

The other condition of success is the localisation of the hole in the retina. Lindner is convinced that tears in the retina exist in every case; where they cannot be seen they either lie too far forward or are covered by a fold. Where the hole cannot be demonstrated, Lindner operates on the assumption that the hole is present in that part of the detachment which appears to have formed first, though it is not always possible to be sure on this point. Of the 11 cases (in the series of 42) in which he could not localise the hole, 8 were submitted to operation, and of these 2 were cured. In Lindner's experience one may assume that no recurrence of the detachment

will take place, if it has not come back within three weeks after the operation, though he saw a recurrence in one case six weeks after an apparently successful operation. Altogether the author has 15 cases of cured detachment, 6 of whom have now been well for over six months.

Some points in the technique of the operation are briefly mentioned, and a special method used by the author for mapping out the localised hole is also touched upon; a reference to a fuller description being given (*Arch. f. Ophthal.*, Vol. CXXIII, p. 233).

ARNOLD SORSBY.

(3) **Meller, J. (Vienna).—The treatment of detached retina by ignipuncture. (Zur Behandlung der Netzhautabhebung mit Ignipunktur).** *Zeitschr. f. Augenheilk*, Vol. CXX, p. 207, 1930.

(3) Since 1925 **Meller** has been treating cases of retinal detachment by ignipuncture, but differing radically from the operation advocated by Gonin, in not attempting to seal any hole that may be present in the retina. He has had 39 patients; 41 eyes showed detachment and 50 ignipunctures were performed. Only five patients were cured, in three of whom the retina has now been re-attached and functioning for over four years, in one for two years, and in the remaining one for over a year. Of these five cases four were myopes, constituting a rather higher rate than was seen in the series as a whole, in which myopia was present in 56 per cent. of the cases.

Meller has not had much success with his attempts to seal the hole in the retina. That it is present, and that it is a primary cause of the detachment he does not doubt, but he points out the great difficulties in hitting on the hole with the cautery. Apart from the problem of finding the corresponding scleral point for any localised retinal hole, there is also the complicating factor, that the escape of subretinal fluid as a result of the scleral incision, prior to plunging in the cautery, must disturb the position of the hole. And yet the hole in the retina is apparently the primary cause of the detachment. Meller found a hole in 66 per cent. of those cases that came to him within four weeks of the onset of the detachment; this high percentage falls steadily with the greater duration of the lesion. In cases seen within two months it had declined to 57 per cent.; to 40 per cent. in cases of over two months and under six; and after the detachment has been present for six months a hole could be seen in only 28·5 per cent. If the hole were a secondary effect due to contraction and shrinking of the detached tissue, its frequency would increase and not decrease with the greater duration of the lesion. That holes are less frequent in cases of long

standing must not be taken to imply that healing takes place; there is no evidence for such a view. It is more likely that the hole becomes hidden by a fold, as was indeed demonstrated in a case of the author, where ignipuncture produced a flattening of the detachment and revealed a hole previously not seen. Whilst Meller does not exclude the existence of holes as secondary features due to shrinking, he sees further evidence as to the primary nature of holes in the facts that the premonitory symptoms of detachment are often associated with small vitreous and retinal haemorrhages, and also that when a detachment re-forms after ignipuncture, it can be seen to begin at the tear in the retina.

The closure of the hole would therefore seem to be an essential part of a successful operation, and Meller is indeed struck by the difference in the results he obtains when the hole is hit upon by the cautery. He discusses the different methods by which this could be achieved, such as using a large-pointed cautery, instead of the very fine one generally employed, or by guiding the point in different directions, or cauterising for a longer period of time than the one second generally allowed. The disadvantages of a larger scar would appear to lie in the possibility of the scar itself acting as a cause of detachment, for even the minute scar due to a point cautery can cause radial folds around it, and lead to serious consequences. Yet two cases with large scars, one Lindner's and the other the author's, have done well. The author's case was one in which the large scar was accidental; it followed on a profuse haemorrhage in the vitreous, after ignipuncture. But whether the sealing of the hole is the primary cause of success in operation is still an open question. The most important contributory factor is probably the smoothing out and relaxation of the detached retina. This view would explain why Deutschmann gets successful results by a procedure exactly the contrary to Gonin's, for Deutschmann makes holes in the retina by one or more incisions. It is possible that a satisfactorily reposed retina will become re-attached and any hole present obliterated by adhesion to the underlying tissue. But on the whole Meller leans toward Gonin's view.

Meller also discusses the danger of profuse haemorrhage as a result of these operations, bleeding being less likely in employing cautery than in using the knife. One case of immediate bleeding did very well, the haemorrhage helping to close the hole in the retina; late bleeding occurred in four cases, and they all did badly. In one case a curious accident happened; the cautery hit on a branch of the central vein, and produced thrombosis in it, but ultimately circulation became restored.

Though the author sees much evidence to support Gonin's theory, he does nevertheless hold that some cases of detachment

are not due to retinal tears, but are caused by inflammatory exudates, which lift and detach the retina. Choroiditis, in his opinion, does not infrequently lead to these serous detachments, and in one case where the lesion was clearly secondary to choroiditis, diagnosed as of tuberculous nature, conservative treatment with anti-tuberculous measures gave " an excellent result."

ARNOLD SORSBY.

(4) **Sourdille, M. G. (Nantes).—Remarks on the pathology and treatment of detachment of the retina. (Remarques sur la pathogenie et le traitement du décollement de la rétine).** *Bull. de la Soc. d'Ophtal. de Paris,* 1929.

(4) After a brief résumé of his ten years work on detachment and its treatment, and of the recent method of Gonin, **Sourdille** considers at length the question of the rôle of the ruptures so frequently seen. von Graefe who first recorded them considered that they were accidental, produced by the pressure of the subretinal fluid, on an already diseased retina. Leber as a result of his observations in a case of a patient with a foreign body in the globe who developed vitreous bands, was led to perform some experiments on animals, and formulated his " théorie de l'attraction." The vitreous bands by contraction tore a hole in the retina, and allowed the vitreous to detach the inner from the outer layers. Later Leber renounced this theory, but evolved one in which numerous pre-retinal bands of extreme tenuity were responsible for the ruptures.

Many objections to these two theories were noted in papers on the subject. In 1920 Gonin revived the second of the two ideas as a result of the pathological investigation of eyes which had been the subject of detachment for a long period, and later enucleated. Sourdille considers that these bands are the result of degeneration, and would not be found in the early stage. He points out that Vogt could find no bands in the vitreous in his examination of numerous eyes with retinal detachment. He quotes Weekers who in 1925 produced experimentally retinal detachments in rabbits by means of the superficial application of the cautery, and who found retinal tears in some only, and considered that they resulted in those cases in which the detachment was rapid and forceful, and that they had nothing to do with the condition of the vitreous.

Sourdille has noticed that in recent detachments there is a higher percentage of tears than in old detachments, and considers that some of them close themselves, but notes that this does not necessarily cure the detachment.

The method which Sourdille has used for many years with great

success depends on the acknowledged clinical fact that there is fluid in between the layers of the retina. This must be removed, and the retina pegged down at certain points. The fluid can be evacuated outside the globe or into the vitreous; hence the presence of a tear is no disadvantage, and in fact the detached layers of retina are perforated again to facilitate this evacuation.

The method has three main stages.

1. Puncture of the sclero-retina in the centre and each side of the detachment with a narrow knife, a centimetre of the blade at least being introduced to perforate the retina.

2. Production of a reaction sufficient to produce adhesion of the retina and choroid, either by a very fine cautery in shallow detachments, or by the injection of cyanide of mercury in deeper ones.

3. Immobilisation of the patient in the position which will most satisfactorily help replacement of the detached retina: half sitting for the lower detachments, on the side for the lateral ones, etc.

Sourdille deprecates the very violent reaction of a larger cautery in the vitreous, as it is liable when the scar forms to cause a further detachment by bands, and he quotes Gonin who in 1921, pointed out that the vitreous is liable to be damaged by the cautery, and a detachment appear at the opposite pole of the globe.

After a review of the cases operated on by Gonin's method, Sourdille gives his own figures for his cases since 1923, and in conclusion he gives as his opinion that the cures by Gonin's method are not due to a closure of the hole, but because the method has produced a sufficient reaction in the choroid to provoke adhesions, and he points out that his own figures of cures have been obtained in spite of the fact that he not only does not close the hole which may or may not be present, but that he makes fresh ones.

O. GAYER MORGAN.

II.—THERAPEUTICS

(1) **King, Clarence (Cincinnati).—The therapeutic value of tuberculin in ophthalmology.** *Arch. of Ophthal.*, June, 1929.

(1) King's paper gives a fairly comprehensive survey of the literature on this subject and an account of his own experiences with thirty-seven cases of ocular tuberculosis, some of them observed over a period of years. That the administration of tuberculin is not such a simple matter as some would think, is evidenced

by a quotation from Ranke " It is possible by tuberculin to change a relative beneficent immunity into the specific toxin hypersensitiveness of the immune." In other words, its use does not imply the introduction of a protective agent, but rather the provoking of a disease. In spite of these statements, however, Ranke held that the proper therapeutic use of tuberculin was only a matter of time. Numerous studies have been made on the subject. von Hippel in 1914 was relatively optimistic in that he reported 75 per cent. of 243 patients as being cured by its use. Bernheimer found that in tuberculous keratitis, during the 6 years when specific therapy was employed there were 20 per cent. of recurrences, whereas in the previous five years, when tuberculin was not used, they amounted to 50 per cent. Hertel as a result of a survey of cases concluded that the general average therapeutic effectiveness of tuberculin as contrasted with non-specific treatment, amounted to 20 per cent. Hess on the other hand found that tuberculin was devoid of influence on ocular tuberculosis and Gilbert in the Graefe-Saemisch " Handbuch " displayed a similar pessimism. There are many more authorities quoted, some in favour of and others against the use of tuberculin. The matter has also been tackled from the experimental side. Hertel, who summarised the results of other workers, concluded that it was not possible to effect a cure with tuberculin in ocular tuberculosis experimentally produced by inoculation. The author feels, however, that these results are not significant because there is no parity between primary inoculation in a non-infected animal and ocular tuberculosis in man, as ordinarily encountered. The latter is usually due to metastasis and variations in the resulting lesion are dependent on the allergic state of the patient at the time of the metastasis. As a result of his personal experience, King is convinced that after treatment with tuberculin, a large proportion of his patients have been able to pursue occupations involving strenuous use of their eyes, whereas before, they were disabled by frequent recurrences. Tuberculin is not, however, suitable for all types of cases and is regarded by Werdenberg as being contraindicated in the highly allergic exudative lesions occurring in the stage of hypersensitiveness, but as indicated in the nodular proliferative, slightly allergic lesions with diminished hypersensitiveness. Stock on the other hand advocates empiricism and maintains that the competent clinician will intuitively resort to the proper treatment after careful observation. From the diagnostic standpoint, it is worthy of note that X-ray examination yields positive evidence of tuberculosis of the pleura in all cases of ocular involvement. With regard to the types of tuberculin, the author considers Toenniessin's tebeprotein as having distinct advantages over other varieties, in that

it is ten times less toxic and has a much greater specific effectiveness. It is also said to be a pure chemical substance, soluble, uniform and susceptible of exact dosage. The diagnostic dose is 0·1 mg. and the initial therapeutic dose 0·001 mg. It is in routine use at Meller's clinic.

F. A. W.-N.

(2) **Young, George (Colchester).—An obstinate case of chronic infection of the conjunctivae from bacillus xerosis.** ***Arch. of Ophthal.***, June, 1929.

(2) **Young** reports an interesting case of chronic conjunctivitis, in which the only organism present was b.xerosis, which was found in very large numbers. It was noticed that the cultures failed to grow on any medium that was slightly acid. All the usual lotions and drops were tried without any effect and the irritation produced by any acid was intolerable. Fresh lemon juice, however, in a strength of 1 or 2 per cent. did not cause irritation and the following prescription was eventually worked out.

	Gm. or c.c.
Boric acid crystals	4·0
Sodium chloride	2·8
Filtered lemon juice	2·0
Suprarenaline (A + Co.)	2·0
Camphor water	50·0
Distilled water to make	200·0

S: to be used frequently, at least three times a day in an eyecup.

The use of this lotion kept the conjunctivitis at bay and rendered the patient completely comfortable. On one occasion, citric acid was substituted for lemon juice with the result that the patient suffered agonies.

F. A. W.-N.

III.—MUSCLES

(1) **Schaeffer, H. and Blum, J.—The syndrome of Parinaud. (Le Syndrome de Parinaud).** ***Arch. d'Ophtal.***, June, 1929.

(1) The outstanding features of this syndrome, total or partial loss of vertical ocular movement, sometimes associated with paralysis of convergence, were first fully described in their clinical

aspects by Parinaud in 1883, although the condition had been noted earlier by other observers (Henoch, 1864: Priestley Smith, Wernicke, 1876).

In the partial form upward rotation alone may be limited and this variety seems from published observations to be the most common: limitation of downward movement alone is not very infrequent, and in the complete form there is simultaneous though not equal loss of all vertical movement.

In a long thoughtful paper the authors " far from attempting to solve many of the undetermined problems," discuss the syndrome and its associated and underlying conditions in the light of present day knowledge.

The clinical examination of these cases demands a careful technique, as described by the writers, by reason of the fact that in some instances the paralysis is one of voluntary movement while involuntary reflex movement is unaffected. This dissociation has been recorded by many observers and has led to much discussion concerning its pathogenesis.

While loss of vertical deviation may be an isolated symptom, it is frequently associated with other neurological signs, some of which have a notable localising value. Among these are loss of lateral ocular movement, loss of oculo-palpebral synergy, nuclear paralysis generally involving the third pair, hemiplegia with unilateral third nerve paralysis. Leri maintains that in almost all cases of paralysis of vertical movement the third pair of nerves are more or less affected. This statement is important, since if an actual fact, it supports the suggestion that in the majority of cases the causal lesion of Parinaud's syndrome is situated in the immediate neighbourhood of the third pair. The symptom indicating involvement of the third pair is diplopia. Hemianopia is an exceptional concomitant condition.

The results of post-mortem examinations hitherto made are of unequal value, the majority having been only macroscopic and very incomplete. Moreover, in several of the recorded cases a neoplasm has been found, often so widespread as to render localisation impracticable.

In the greater number, however, lesions have been found involving the corpora quadrigemina or the immediately adjoining structures, less commonly the optic layer and the region of the aqueduct of Sylvius, the peduncle, the nucleus of the third pair, and the pons. It is noteworthy that in a certain number of cases the corpora quadrigemina were intact, and the opinion is held that the rôle of the corpora in associated movements of the eyes is very uncertain. Bernheimer has shown that such movements can be excited by stimulation of the cortex after destruction of the corpora

quadrigemina, and Ferrier and Turner are of opinion that lesions of these bodies give rise only to transient disturbances.

The complexity of vertical movements including as they do voluntary, associated, and automatic movements, differing both physiologically and phylogenetically, is obvious. It is logical to assume that the lesion which determines paralysis of such movements, singly or grouped, does not invariably occupy the same site. It seems equally reasonable to admit that paralysis of automatic movement is dependent upon a lesion which isolates the nuclear or paranuclear centres from the various centres of reflex excitation (optic, acoustic, labyrinthine, cervical, tactile); and that paralysis of voluntary movement arises from interruption of the connections between the oculo-motor nuclei and the cortex, such interruption being very probably bilateral. This hypothesis, for it is no more than an hypothesis, requires confirmation by clinical and anatomical examinations conducted with meticulous care and accuracy.

J. B. LAWFORD.

BOOK NOTICES

Cuénod et Nataf (Tunis): Le Trachome. Paris: Masson. 1930. 50 francs.

Having read this book through with great interest the reviewer may state that it is possible to learn all about trachoma from this well-printed and well-illustrated volume, which is sold for eight or nine shillings. It is well documented, and sufficiently up to date to refer to the discussions on trachoma at the International Ophthalmological Congress at Amsterdam in September last.

Cuénod and his assistant, Nataf, have studied the disease in Tunis for many years, where its ubiquity resembles the conditions in Egypt. Cuénod is well known from his association with Charles Nicolle, the Director of the Pasteur Institute at Tunis, in important experimental work on the production of trachoma in monkeys.

The clinical description of the various forms of the disease is very good. It is based on MacCallan's classification of the stages of trachoma. Trachomatous granulations of the superior convexity of the cornea, and their resulting depressed scars, are attributed to another than Herbert, for their first description. It will be remembered that a full description of this condition was given by Herbert in the *Transactions of the Ophthalmological Society of the United Kingdom* for 1904.

The conditions resulting from accidents at work by persons who have either active or undiagnosed trachoma are very important; in the case of an active trachoma the condition may become very much worse with fresh ulceration of the cornea, while in the case of a person who has a quiet and undiagnosed trachoma a veritable explosion may occur, the unsuspected initial stage of trachoma (Tr. I) rapidly developing into the generalised stage of large follicles (Tr. II), with great increase of pannus. Very difficult compensation cases may be brought into Courts of Law on this account.

Cuénod's extensive experience in the treatment of trachoma merits that his method of dealing with confirmed cases of the disease (Tr. II), should be described. Those who see only sporadic cases of trachoma should satisfy themselves that they are not dealing with a case of Tr. III with old protective pannus, before adopting an extremely severe method of treatment, well adapted though it may be to Tunisians or other hardy African races, in suitable cases.

The method is as follows:—After infiltration anaesthesia of the upper and lower lids and of the subconjunctival tissue of the eyeball, the whole of the conjunctiva is very thoroughly curetted. Then a subconjunctival injection of cyanide of mercury, 0·2 per cent. solution, is made under both palpebral and bulbar conjunctivae. After this an energetic massage of the palpebral conjunctiva with powdered boric acid is carried out. Excess of boric acid is washed away with a solution of copper sulphate and the eye is occluded with a pad and bandage, after instilling atropine, and plenty of ointment containing camphorated copper. The operation is completed by injecting subcutaneously into the arm a little of the material removed during the curettage, with the idea of producing, if possible, the formation of antibodies.

This heroic treatment demands, it would seem, the soul of a martyr in the patient, as the after treatment demands the daily passage for four days of a glass rod, carrying ointment, through the fornices, in order that symblepharon may be avoided.

The final results are said to be good. It is advisable to operate on only one eye at a time.

Treatment by chaulmoogra oil has not been very satisfactory.

Treatment of trachoma by diathermy has been advised by some authors but not by Cuénod; as he says, very rightly "la diathermie peut provoquer de véritables dégâts post-opératoires."

The aetiology of trachoma, according to the authors, may be summed up in the statement that it is a specific, contagious disease, localised in the conjunctiva of man, transmissable by inoculation to certain kinds of monkeys, and caused by a filtrable virus. These

researches were carried out under the high authority of Nicolle, by Cuénod and Blaizot.

As regards the bacteriology of the disease the authors adopt a non-committal attitude as to the specificity of the bacterium granulosis described by Noguchi. They are inclined to the belief that one or more bacteria are involved, which are carriers of an ultramicroscopical virus.

The book is written with the greatest clarity of expression and can be comprehended by any one with a small knowledge of the French language. However, it is to be hoped that an English translation will soon be available for Americans, Indians, Egyptians, and others who have to deal with trachoma " en masse."

Giza Memorial Ophthalmic Laboratory, Cairo. Third Annual Report. Cairo: Misr Press.

This volume of 112 pages is written by the Director of the Laboratory, Mr. Rowland P. Wilson, who gives an account of the foundation. " It stands as a token of Britain's esteem of Egypt's dead, and is a worthy monument, for it is probably the finest ophthalmic laboratory in the world. The funds for its erection were voted in 1921 by the Imperial War Graves Commission in London. The income of the Laboratory is derived from three sources, the interest from the original trust fund established by the late Sir Ernest Cassel for ophthalmological work in Egypt, the interest from a trust fund established by the British Red Cross for the benefit of the poorer classes of the country, and a grant from the Egyptian Government. The Laboratory is truly a magnificent building, often quoted as being one of the finest examples of modern architecture in Egypt, and is enhanced by its situation near the western bank of the Nile, and on one of the main routes to the Giza Pyramids. Being in a central position in the country and adjoining one of the largest of Egypt's ophthalmic hospitals, where more than 20,000 new cases are treated a year, it has access to clinical material such as is possessed by few other ophthalmic hospitals in the world." The annual expenses of the Laboratory are about £6,000.

At this Laboratory the routine pathological work is carried out for the 41 ophthalmic hospital units which now exist in the country, of which 27 are permanent built hospitals and 14 are travelling hospitals under canvas, according to 1928 statistics.

Two courses of instruction for the medically qualified Egyptians who are taking up special ophthalmic work are held every year, after each of which there is a searching examination, which must be passed with credit.

Admirable facilities for research work are present and full use of these has been made by Mr. Wilson and his fellow workers.

In the Report, which is well printed and illustrated, there is much interesting material, but coming from Egypt interest is naturally centred on the trachoma problem. Mr. Wilson has not, as yet, been able to confirm Noguchi's work as to a specific organism.

The main points of Noguchi's work are recalled here. In 1926 he isolated an organism from four pupils in an Indian School in New Mexico where trachoma is endemic. The diagnosis in these cases was confirmed by Lindner. Inoculation into certain monkeys induced a conjunctivitis, with follicles developing after two to four weeks. In one case scar formation occurred within eight months. Histologically the lesions in the monkey closely resembled those commonly found in American Indian trachoma. The disease was transmitted from one monkey to another and the micro-organism was recovered from the experimental lesions.

The characters of Noguchi's organism were as follows:—After adaptation to artificial cultivation it had a superficial resemblance to the xerosis bacillus and other diphtheroids, but is Gram-negative, decidedly smaller, and under certain conditions, motile. The initial cultures were obtained only on leptospira media and on blood-agar plates containing certain carbohydrates.

Wilson isolated a similar organism and reported in March, 1928, on its tendency to develop Gram-positive characters. This is confirmed by Morax in *Revue International du Trachome* for January, 1930, where he states definitely that the organism in a culture obtained from the Rockefeller Institute, according to the methods of staining employed at the Pasteur Institute, is Gram-positive, and not Gram-negative as stated by Noguchi. However, Wilson regards the organism he found as mainly Gram-negative.

Inoculation of the conjunctiva of monkeys with the Gram-negative bacillus produced a follicular conjunctivitis, but not trachoma. The paper should be read in its entirety by trachomatologists.

Bulletin of the Ophthalmological Society of Egypt. Cairo: Misr Press. 1929.

The Ophthalmological Society of Egypt is a flourishing one and has now 137 full members. Financially it has a gratifying credit balance. The " Bulletin " is well printed and has a number of good illustrations.

Among other papers of interest is one by Dr. M. A. Barrada on a number of cases of proptosis which he has seen recently.

Mr. Rowland P. Wilson has an interesting paper on hysterical disorders of the eye. One of the cases described had increased intra-ocular tension and a restricted visual field in one eye. After a period of treatment the condition became normal, and after a year's interval complete normality remained.

Annual Report of the Department of Health, Government of Palestine. 1928.

In this Report Colonel Heron, the Director of the Department, comments on the growth of work carried out by the six ophthalmic clinics established in 1924. The number of new cases has doubled in the last three years, and now amounts to more than 18,000 per annum. These clinics are intended to deal chiefly with trachoma, acute conjunctivitis and the complications and sequelae of these diseases. Cases for diagnosis or for intra-ocular operation are transferred to the Ophthalmic Hospital of the Order of St. John, at Jerusalem.

Nearly 80 per cent. of the patients were trachomatous. 1,182 operations for trichiasis were performed. It is as yet impossible to deal completely with the stream of trichiasis-entropion cases which arrive at the clinics in need of operation.

Pharmacopoeia of the Central London Ophthalmic Hospital. London: H. K. Lewis & Co., Ltd. 30pp. Royal 32mo. 1930. Price, 2s.

The Central London Ophthalmic Hospital Pharmacopoeia is a well got up volume of a size convenient for the waistcoat pocket, and interleaved. It contains all the usual formulae for topical application as well as a convenient assortment of pills and powders together with a liberal number of misturae, and a useful table of approximate equivalents. The ophthalmological student, with this little book at hand, may well feel that he is like Habakkuk, " capable of anything," at least in a therapeutic sense.

NOTES

Death WE regret to record the death of Dr. A. Bietti, director of the Ophthalmological Clinic at Bologna, at the age of 60 years.

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Honour DR. V. MORAX has been elected a member of the Académie de Médecine in the surgical section.

Gifford Edmonds' Prize

THE prize for the year 1930 offered for an essay on "Central Scotoma, its Pathology and Clinical Significance" has been divided between Rosa Ford, M.B., of London, and Laura M. Ligertwood, F.R.C.S., of Edinburgh.

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Penal Blinding

A STORY in "Matthew of Westminster," retailed in Holinshed's Chronicles, has some bearing on this subject and may be of interest to our readers. In 1107 Robert, Duke of Normandy, the Conqueror's eldest son, was taken prisoner by Henry I, his brother, and committed to prison in the castle of Cardiff. One day he attempted to escape, but was recaptured. "His keepers kept him in close prison, advertising the king of his demeanour: whereupon he commanded that the sight of his eies should be put out, but so, as the balles of them should remain unbroken, for the avoiding of a noisome deformitie that otherwise would ensue, if the glassie tunicles should take hurt." The unfortunate Robert would appear to have been treated much as decoy birds were, by "stinging out the eyes with a red-hot needle," to make them sing automatically. The early appreciation of the deformity caused by a bilateral excision is interesting.

FUTURE ARRANGEMENTS

1930

June 3.—Midland Ophthalmological Society, at Worcester.

June 13.—Section of Ophthalmology, Royal Society of Medicine. (Annual Meeting.)

July 10-12.—Oxford Ophthalmological Congress, at Oxford.

August 26-29.—British Medical Association, at Winnipeg.

October 7.—Midland Ophthalmological Society, at Birmingham.

December 2.—Midland Ophthalmological Society, at Birmingham.

CONTEMPORARY OPHTHALMIC LITERATURE

American Journal of Ophthalmology. *April, 1930.*

KLAUDER and ROBERTSON. The Wills Hospital Clinic for the treatment of ocular syphilis.
CLAPP. A case of tuberculous retinitis.
GREENWOOD. Combined iridencleisis and sclerectomy for chronic glaucoma.
GRADLE. Ignipuncture in detachment of the retina.
FOX. Peridectomy.
AGATSTON. Retinal angiospasm: its relation to arteriolar disease.
WEYMANN. Scleral cyst of traumatic origin.
MATHEWSON. A case of extreme megalocornea.
STIEREN. Amblyopia from ingestion of gelsemium contained in a nostrum.
JACKSON. How to use the cross cylinder.
DAVIDSON. Eye examination record and topographic chart.
TASSMAN. A case of Krükenberg spindle.

Archives of Ophthalmology. *March, 1930.*

GAY. The treatment of ocular tuberculosis with tuberculin.
GOLDSTEIN and WEXLER. Melanosis uveae and melanoma of the iris in neurofibromatosis (Recklinghausen).
GREEN, A. S., L. D. and M. I. Glaucoma: factors underlying success in trephining.
McKEE. Blastomycosis of the eye.
PILLAT. Leprosy bacilli in the scraping from the diseased cornea in a leper, and comments on keratitis punctata superficialis leprosa: report of a case.
ADLER. Reciprocal innervation of the extra-ocular muscles.
COWAN. Subconjunctival injection of Pregl's solution in gonorrhoeal ophthalmia.
FREEMAN. The extent of the field of vision in lens micropsia.

Annales d'Oculistique. *March, 1930.*

QUIDOR and HÉRUBEL. Visual perceptions.
——— Registration and projection of colour relief.
CHAILLOUS and GARNIER. Clinical study of some cases of retinitis in hyperglycaemics who have become aglycosuric.
AURAND. New method of replacement of the oblique muscles by double oblique convergent advancement of their re-doubled synergic muscles. (External rectus and superior or inferior rectus).
AGNANTIS. Palpebro-superciliary autoplasty.
SALVATI. The treatment of squint by injections of alcohol.

Archives d'Ophtalmologie. *April, 1930.*

WORMS and SOURDILLE. The importance of papilloedema in the diagnosis between epidemic encephalitis and cerebral tumour.
VILLARD. The ocular complications of malaria.
SÉDILLOT. Anatomical and clinical proofs of the pituitary mechanism in ophthalmic and ophthalmoplegic migraine.
DEJEAN. Bi-nasal hemianopia.
TOULANT. Vaccinal keratitis.

Revue d'Oto-Neuro-Ophtalmologie. *January, 1930.*

NORDMANN. On the pathology of optic atrophy in oxycephaly.
ROGER. Acute neuro-optico-myelitis with precession of slight medullary disorders.
NORDMANN and METZER. Concerning a case of disorder of associated movements of the eyes with retractor-nystagmus and dissociation of vestibular nystagmus.

Klinische Monatsblätter für Augenheilkunde.

April, 1930.

IGA. On the focal reaction in the untouched eye after parenteral use of foreign serum.
KUBIK. On the underlying cause of the Kayser-Fleischer ring in pseudo-sclerosis.
WAARDENBURG. On the combination of total colour blindness and retinal atrophy in one person with observations on congenital achromatopsia and the yellow pigment of the macula.
GNAD. On the method of action of pupillo-motor drugs according to the exact locality of application.
RIEGER. On a case of medullated nerve fibres in the papillo-macular bundle with high myopia and macular changes.
GYGER. On the bearing of medullated nerve fibres in the retina in Recklinghausen's disease.
MEYER. Lens myopia from congenital microphakia.
BERND. Bi-lateral aplasia of the first division of the fifth nerve with retained secretion of tears.
HERZOG. Hereditary congenital optic atrophy.
WOLCHONSKY. Prowazek's bodies in trachoma.

Zeitschrift für Augenheilkunde. *April, 1930.*

KRASSO. The treatment of diseases of the anterior portion of the eye with Bucky's rays.
JAENSCH. On the therapy of tabetic atrophy.
PILLAT. On the diagnosis by similarity of eye symptoms in uniovular twins and on ophthalmoscopic symmetry of certain signs.
KRONFELD. The retention of the intra-ocular pressure after opening of the anterior chamber in glaucoma.
HEIMANN. The grounds for physico-dietetic treatment of glaucoma.

Annali di Ottalmologia e Clinica Oculistica. *February, 1930.*

CIRINCIONE. Precision in the treatment of eye diseases.
LO CASCIO. Modern views on the sensory mechanism of vision.
SANTONASTASO. Contribution to the study of rare forms of syphilis localised exclusively in the eye.
FRATICELLI. Notes on a report of Prof. Cirincione. (Note).
PUGLISI-DURANTE. Histo-clinical contribution to the study of the routes of extra-bulbar spread of melanotic sarcoma of the choroid.
MUREDDU. On the numerical connection between the visual cells and ganglion cells of the human retina.
CASO. Insulin therapy in ocular lesions.
CATTANEO. On operative interference in dacryo-cystitis.
PANICO. Primary carcinoma of the cornea.

Archivio di Ottalmologia. *February, 1930.*

SGROSSO. Perithelioma of the orbit and the bulb.
NICOLATO. Extraction of the transparent lens in the surgical treatment of keratoconus.

Rivista Oto-Neuro-Oftalmologica. *January-February, 1930.*

DI MARZIO, On ocular paralysis following spinal anaesthesia and lumbar puncture.
SABBADINI. On recurrent serous meningitis with particular regard to the ocular symptomatology.
DE ANGELIS. Contribution to our knowledge of meningioma of the parietal lobe.

Annales de Oculistica do Rio de Janeiro. *February, 1930.*

MATTOS. Serous cyst of the iris.
SIMÕES. On electrical ionisation in cataract.
PEREIRA. Paroxysmal attacks of hypertonia with conjugate deviation of the head and eyes. Post-encephalitic Parkinsonianism.
NEURAUTER. Trans-sphenoidal fissure with serous arachnoiditis of Uhthoff.

March, 1930.

DE ABREU. The eyes in forensic medicine.
DE ANDRADE. Exudative choroido-retinitis and hypertrophic maxillary sinusitis.

Revista Oto-Neuro-Oftalmologica y de Cirugia Neurologica.

February, 1930.

LUQUE and DRECKMANN. Functional strabismus in an adult.
PINES. Sclerosis of the retinal vessels.
ONFRAY, GOULFIER and COUDRAY. Paralysis of the downward movements of the eyes.
HESS. Experiments in localisation of cerebral excitation producing sleep.

March, 1930.

PINES. Sclerosis of the vessels of the retina.
SEGURA. Ophthalmic complications of scarlet fever.
COLRAT. Atypical scotoma in a case of chiasmal syndrome.
GAMA. Perfecting the technique of alcohol injection of the Gasserian ganglion

Anales de la Sociedad Mexicana de Oftalmologia y Oto-Rino-Laringologia.

August-September, 1929.

GONZALEZ. Medical treatment of ocular syphilis.

October-November, 1929.

GONZALEZ. Medical treatment of ocular syphilis.

December, 1929.

GONZALEZ. Medical treatment of ocular syphilis.
AVALOS. Some applications of auto-haemo-therapy in ocular therapeutics.